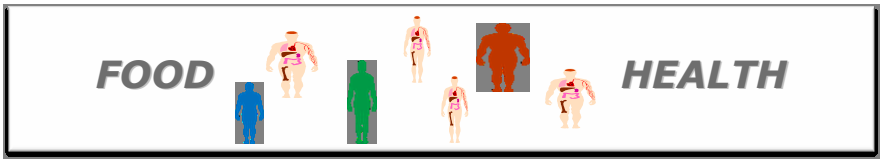
Winterschool: Overview of the field of bioactive compounds

DHI & ØFN 2009-10

KU-Life 03-11-2009

Overview of bioactive compounds: experience from industry and university



LIFE, University of Copenhagen
Council for Strategic Research
ActiFoods ApS

Peter Olesen

ActiFoods

Ministeriet for Videnskab Teknologi og Udvikling

Food and health: the functional paradox

'normal foods'

Intrinsic health functionalities

'functional foods'

Modified/added functionalities

- ***ALL FOOD IS FUNCTIONAL***
- ***POSITIVE & NEGATIVE EFFECTS***
- ***AND DIFFERENT FOR YOU AND ME***

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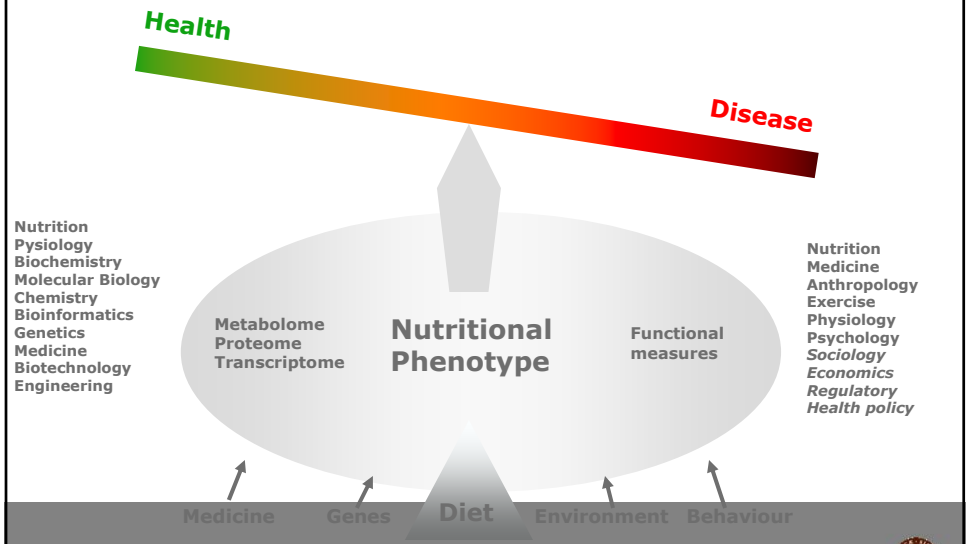
A complexity and multidisciplinary issue



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From: Steve Zeizel et al., 2005

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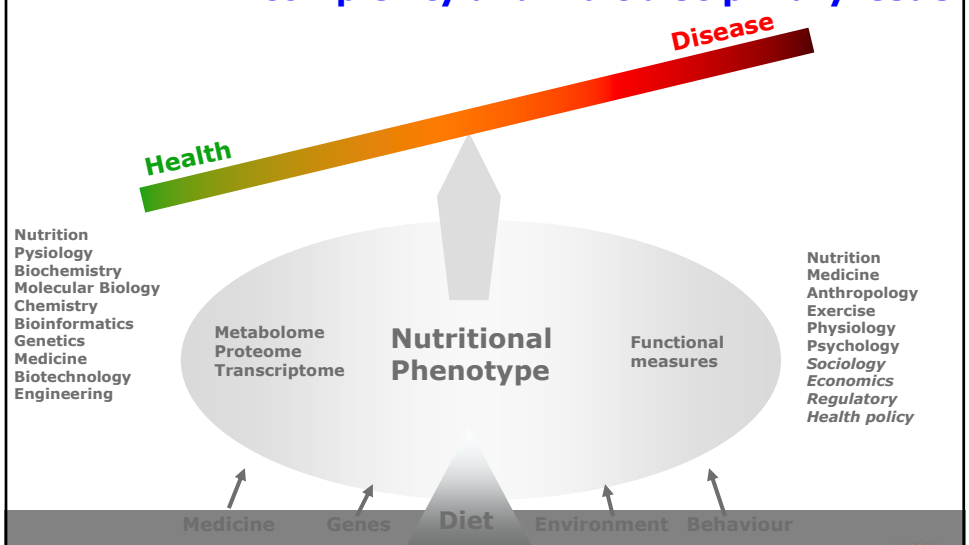
A complexity and multidisciplinary issue



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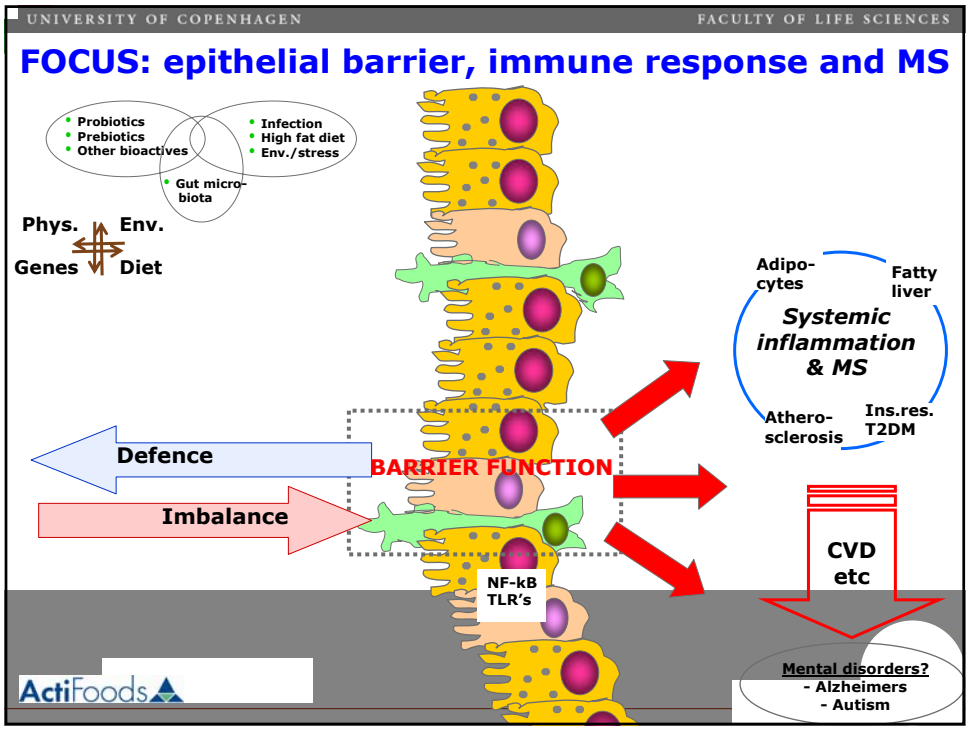
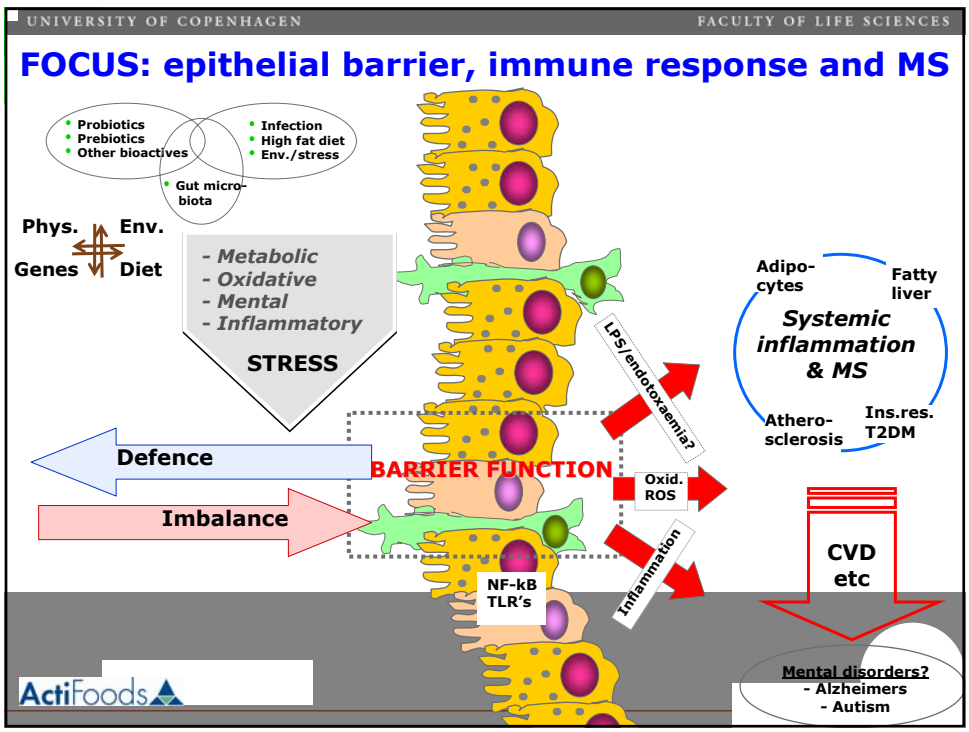

UNIVERSITY OF COPENHAGEN
FACULTY OF LIFE SCIENCES
FOCUS: epithelial barrier, immune response and MS
Probiotics
Prebiotics
Other bioactives
Infection
High fat diet
Env./stress
Gut micro-biota
Phys.
Env.
Genes
Diet
Adipo-cytes
Fatty liver
Systemic inflammation & MS
Athero-sclerosis
Ins.res. T2DM
Defence
Imbalance
BARRIER FUNCTION
NF-kB TLR's
CVD etc
Mental disorders?
- Alzheimers
- Autism
ActiFoods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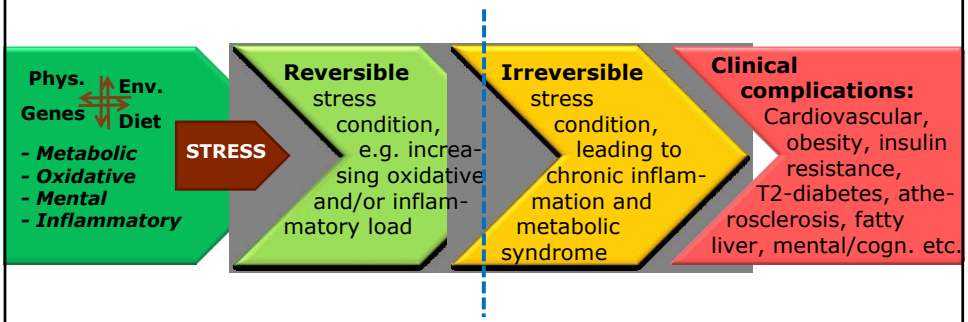
HEALTH = not just the 'absence of disease', but the organism's ability to maintain metabolic homeostasis (balance)



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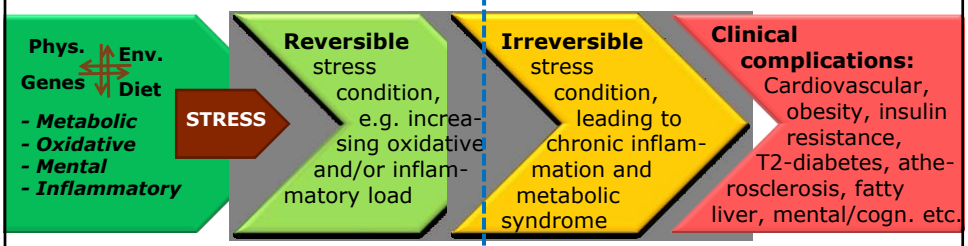
HEALTH = not just the 'absence of disease', but the organism's ability to maintain metabolic homeostasis (balance)



HEALTH – ability to counteract the reversible stress condition ~ 'metabolic plasticity'

DISEASE – irreversible progress into metabolic syndrome and, potentially, clinical complications

Major classes of health-related plant bioactives

- Flavanoids a.o. Phenolics*
- Carotenoids
- Plant sterols
- Glucosinolates in brassica's
- Other sulphur compounds

*Most groups consist of many sub-categories, e.g. antocyanins, isoflavones, flavones, flavanones, flavan-3-ols and flavonols are sub-groups of flavonoids

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Commonly proposed mechanisms of antioxidants a.o. plant bioactives in protection against chronic diseases

- Detoxification of cancer-causing agents (activation of Phase I/II detoxification enzymes
- Causing cancer cells to die (apoptosis / suppression of mitosis)
- Influencing cell-to-cell communication
- Modification of hormonal profile (e.g. steroid hormone levels)
- Modification of lipid profile
- Protection against DNA damages causing abnormal gene expression / increasing DNA repair
- Stimulation of the immune system
- Anti-inflammatory effects
- Reducing serum cholesterol
- Antimicrobial activity

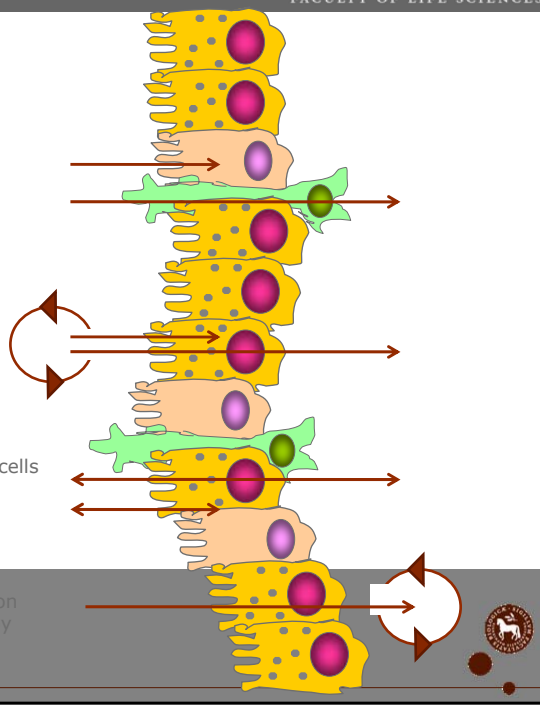
Modes of action for food bioactives

Direct action
- as ingested or bioconverted in gut
  ex: milk peptides
  ex: resveratrol
  ex: antioxidative food

Microbiota
- diversity and dynamics
  ex: chicken flora
  ex: probiotic effects
  ex: prebiotic / synbiotic effects

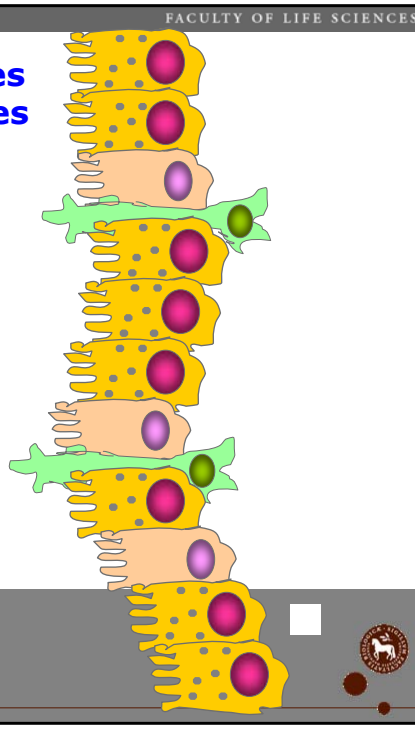
Complex communications
- bioactives/microbiota/host immune cells
  ex: microbial symbiosis factor
  ex: epithelial response factor

Drug interference
- bioactive improving antibiotic function
  ex: flavor compounds and TB therapy



Examples of food bioactives and supposed functionalities

- **Prebiotics**
- **Probiotics**
- **Synbiotics?**
- **Dairy peptides**
- **Resveratrol**
- **Flavour pheromones**
- **Quorum sensing blockers**
- **Sterol/stanol esters**
- **Sterol esters and Ω-3 PUFA's**



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Can Bifidobacteria help prevent development of metabolic syndrome?

High fat diet

- ↑ Endotoxeamia (plasma LPS)
- ↓ Caecal counts – Gram positives – Bifidobacteria

High fat diet + oligofructose

- ↓ Endotoxeamia (plasma LPS)
- ↑ Caecal counts – Gram positives – Bifidobacteria

Both probiotic and prebiotic (synbiotic?) effects

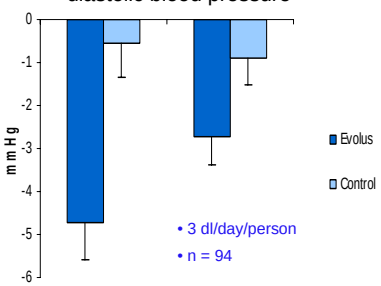
Selective Increases of Bifidobacteria in Gut Microflora Improve High-Fat-Diet-Induced Diabetes in Mice Through a Mechanism Associated with Endotoxaemia
Cani PD et al. 2007, Diabetologia, in press

Modifying the gut microbiota in favour of Bifidobacteria may prevent deleterious effects of high-fat-diet-induced metabolic diseases...

Evolus

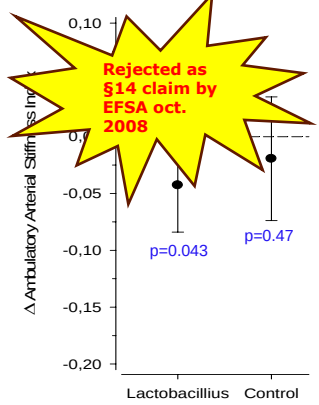
Clinical effects

Changes in systolic and diastolic blood pressure



Jauhiainen et al. Am J Hypertens 2005
Tuomilehto et al. J Hum Hypertens 2004
Seppo et al. Am J Clin Nutr 2003
Seppo et al. Milk Sci Int 2002.

Evolus reduces arterial stiffnes



Jauhiainen et al. Int Dairy J 2007

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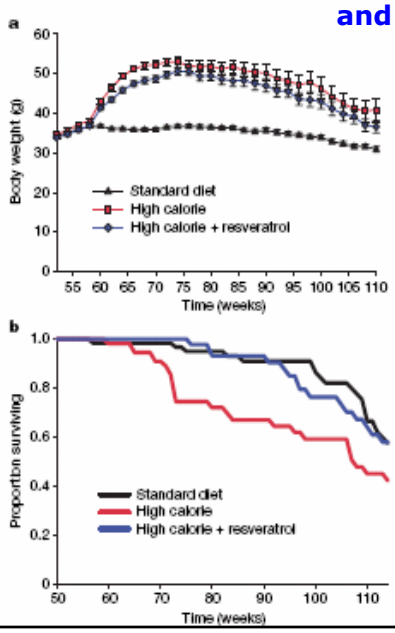
Courtesy of Dr. Tiina Mattila-Sandholm, Valio (Finland)

Dr. Joseph
A. Baur
Harvard Med. School

Resveratrol – a plant polyphenol and anti-oxidant – is anti-inflammatory



Effect of resveratrol on obese mice

Decrease in:
- Inflammation
- Fat accumulation
- Diabetes development
- Liver damage

Increase in:
- Endurance

Resveratrol

- A Danish biotech/nutraceutical company providing a pure, high quality Resveratrol product – a stilbene polyphenol expected to have
  - anti-aging properties
  - cancer preventive activity
  - cardiovascular protective effect
- Recombinant fermentation process in yeast (naturally occurring in grape skin, many plant roots etc.) – probably providing defense against fungal infections
- Scientific indications for
  - estrogenic / antiestrogenic effects in mammary tumor models
  - activator of sirtuin genes, mimics caloric restriction
  - delay of ageing in metazoans (e.g., *C. elegans)*
  - extension of life span in *Saccharomyces cerevisiae*
- W/w > 350 patents filed

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34 Børsen 29-10-2009.

Danskerne er for fede

Mere end hver tredje borger i Danmark vejer for meget. Det er en af de mange konklusioner fra KRAM-undersøgelsen, der på forskellige fronter har inddraget op mod 76.000 borgere for at tage et tilstandstjek på, hvordan det forholder sig med kosten, rygningen, alkoholen og motionen. En anden konklusion lyder, at flere ældre end unge spiser mere fedt end anbefalet, men at flere unge end ældre indtager for meget sukker i forhold til anbefalingerne.

Undersøgelsen slår fast, at danskerne gerne vil deres dårlige vaner til livs. Godt hver tredje person, der ryger cigaretter dagligt, vil gerne kvitte dem, og ca. hver tredje, der spiser usundt, ønsker at spise sundere. Gro

Karry dræber kræftceller

Curcumin er et ekstrak, fundet i det lysegule karrykrydderi, og det kan ifølge forskere fra Cork Cancer Research Center dræbe kræftceller. I hvert fald i de laboratorieforsøg, som forskerne har gennemført.

Nu håber de ifølge British Journal of Cancer, at deres resultat kan hjælpe læger med at finde nye kræftbehandlinger. Forsøget har vist, at curcumin angreb kræftcellerne og dræbte dem inden for 24 timer. Gro

Ballerup er årets cykelby

Cyklerne skal ud af skurene i Ballerup Kommune, der i går blev kåret som »Årets Cykelby 2009« af Dansk Cyklist Forbund. Kommunen med ca. 47.000 borgere tænker cyklismen som en vigtig brik i sundheds-, miljø- og socialpolitikken, og det er denne helhedstænkning, der udløser kåringen. Gro

Filmfestival blænder op for madfilm

»Food Inc.« er en af de kritiske, madfokuserede film, som Copenhagen International Documentary Film Festival Cph Dox viser på årets festival. Filmen er en »dokuthriller« og viser nogle af de økonomiske samt miljø- og sundhedsmæssige konsekvenser af, at forbrugerne sætter billig fastfood til livs.

Efter

Curcumin induces apoptosis-independent death in oesophageal cancer cells

G O'Sullivan-Coyne, G C O'Sullivan, T R O'Donovan, K Piwocka and S L McKenna

Br J Cancer 101: 1585-1595; advance online publication, October 6, 2009; doi:10.1038/sj.bjc.6605308

Abstract

Background: **Oesophageal cancer incidence is increasing and survival rates remain extremely poor. Natural agents with potential for chemoprevention include the phytochemical curcumin (diferuloylmethane). We have examined the effects of curcumin on a panel of oesophageal cancer cell lines.**

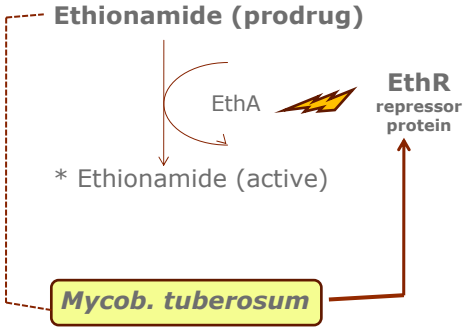
Methods: **MTT (3-(4,5-dimethyldiazol-2-yl)-2,5 diphenyl tetrazolium bromide) assays and propidium iodide staining were used to assess viability and DNA content, respectively. Mitotic catastrophe (MC), apoptosis and autophagy were defined by both morphological criteria and markers such as MPM-2, caspase 3 cleavage and monodansylcadaverine (MDC) staining. Cyclin B and poly-ubiquitinated proteins were assessed by western blotting.**

Results: **Curcumin treatment reduces viability of all cell lines within 24 h of treatment in a 5–50 M range. Cytotoxicity is associated with accumulation in G2/M cell-cycle phases and distinct chromatin morphology, consistent with MC. Caspase-3 activation was detected in two out of four cell lines, but was a minor event. The addition of a caspase inhibitor zVAD had a marginal or no effect on cell viability, indicating predominance of a non-apoptotic form of cell death. In two cell lines, features of both MC and autophagy were apparent. Curcumin-responsive cells were found to accumulate poly-ubiquitinated proteins and cyclin B, consistent with a disturbance of the ubiquitin–proteasome system. This effect on a key cell-cycle checkpoint regulator may be responsible for the mitotic disturbances and consequent cytotoxicity of this drug. Conclusion: Curcumin can induce cell death by a mechanism that is not reliant on apoptosis induction, and thus represents a promising anticancer agent for prevention and treatment of oesophageal cancer**

Drug interference from a food ingredient improves tuberculosis therapy

TB strikes back (WHO data):

- 9.000.000 new cases each year
- 50.000.000 infected with Rifampicin and Isoniazid resistant strains of *Mycobacterium tuberculosum*
- Ethionamid only effective remedy, but fatally toxic at high doses



Weber W et al. (2008) A synthetic mammalian gene circuit reveals antituberculosis compounds http://www.pnas.org/content/105/29/9994

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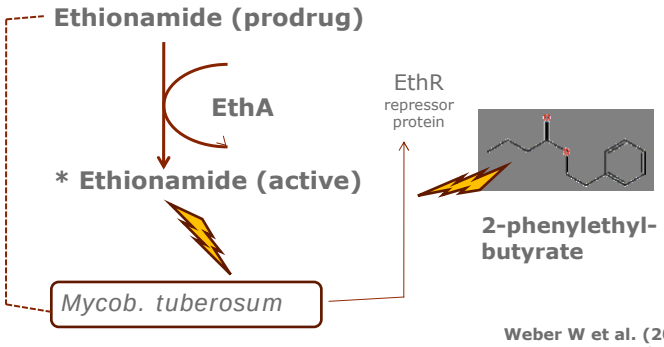

An approved food ingredient
A floral flavor (phero-mone) compound from plants – orchids, citrus, old sherry etc.

Weber W et al. (2008) A synthetic mammalian gene circuit reveals antituberculosis compounds
http://www.pnas.org/content/105/29/9994

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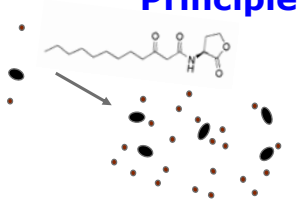
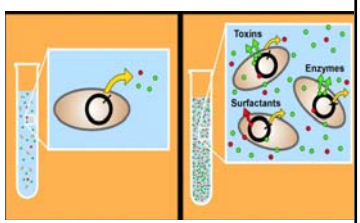
Principle of Quorum Sensing, QS



Increasing cell density and signal concentration



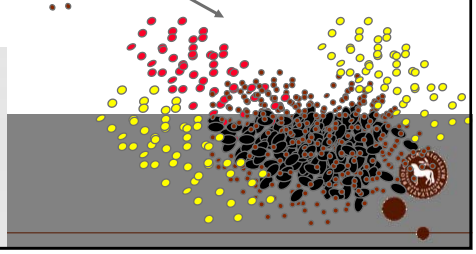
Bacterial cell

Signals

Products

The quorum size is reached

The culture makes "a collective decision" and expresses QS controlled target genes



Original Article — Marine Biotechnology

Quorum Sensing Antagonism from Marine Organisms

Mette E. Skindersoe,[1] Piers Ettinger-Epstein,[2] Thomas Bovbjerg Rasmussen,[1] Thomas Bjarnsholt,[1] Rocky de Nys,[2] Michael Givskov[1]

[1]Department of Bioscience and Technology, Technical University of Denmark, DK-2800 Kgs, Lyngby, Denmark
[2]School of Marine and Tropical Biology, James Cook University, Townsville, Q4811, Australia
[3]Genomics and Strain Development, Chr-Hansen A/S, Boge Allé 10-12, 2970, Hørsholm, Denmark

Received 30 March 2007 / Accepted 20 June 2007

A DSF "FØSU" project that aims at prophylactic 'antimicrobial' diets

Prof. Michael Givskov et al., KU-Sund

- A large number of plant, herbs and food extracts have been prepared from several commercial sources, with varying degrees of biological activity against the quorum sensing inhibition assay.
- Of the 100 + samples investigated for activity to date, about 10% have shown activity against QS. With **garlic and horse-radish,** we have isolated and identified the active ingredients**.**
- Of the remaining active samples**, wasabi, rosemary, water cress, mustard oil, lemongrass oil and pomegranate** have been partially fractionated. Work continues on these samples, to identify the active constituents.









Plasma cholesterol – a validated biomarker for CVD

Ingredient: plant sterol esters

Ingredient: plant stanol esters

- **Plant sterols and stanols are found naturally in the diet in small amounts, such as vegetable oils, legumes, fruit and vegetables, bread and cereals**
- **A daily intake of ~ 2 g can reduce both total cholesterol and (bad) LDL-cholestrol by 10-14% within ~ 3 weeks**
- **Products evaluated and approved as "novel foods" according to current EU-laws**
- **Functional claim, not health claim: "Becel pro-activ® lowers total- and LDL-cholesterol"**
- **Product has to be labelled in such a way that "consumers easily can limit the consumption of the active ingredient to 3 g per day" (SNF)**

ActiFoods

Atherosclerosis 204 (2009) 476–482

Contents lists available at ScienceDirect

Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

Anti-inflammatory and cardioprotective effects of n-3 polyunsaturated fatty acids and plant sterols in hyperlipidemic individuals

Michelle A. Micallef[a], Manohar L. Garg[a,b,*]

[a] Nutraceuticals Research Group, School of Biomedical Sciences, Faculty of Health, University of Newcastle, Callaghan, NSW, Australia
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ARTICLE INFO

Article history:
Received 20 May 2008

ABSTRACT

Background: Risk factors of cardiovascular disease such as lipid aberrations, hypertension, abdominal adiposity and elevations in systemic inflammation, are prominent aetiologies in hyperlipidemia.

Conclusion: We have demonstrated, for the first time that dietary intervention with n-3 PUFA and plant sterols reduces systemic inflammation in hyperlipidemic individuals. Furthermore, our results suggest that reducing inflammation provides a potential mechanism by which the combination of n-3 PUFA and plant sterols are cardioprotective.

Plant sterols

1.4 g/d n-3 PUFA capsules with or without 2 g plant sterols per day.

Results: The combination of n-3 PUFA and plant sterols reduced several inflammatory markers. High sensitivity C-reactive protein (hs-CRP) was reduced by 39% ($P = 0.009$), tumor necrosis factor-α (TNF-α) by 10% ($P = 0.02$), interleukin-6 (IL-6) by 10.7% ($P = 0.009$), leukotriene B_4 (LTB_4) by 29.5% ($P = 0.01$) and adiponectin was increased by 29.5% ($P = 0.05$). Overall cardiovascular risk was reduced by 22.6% ($P = 0.006$) in the combination group.

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Combined effects of n-3 PUFAs (omega-3) and plant sterols - a human intervention study

HYPOTHESIS

- Cardiovascular risk factors tend to cluster in hyperlipidemics
- Interventions targeted at multiple risk factors likely to be beneficial
- Cardioprotective effects would be expected

DESIGN

60 hyperlipidemics*

male n= 27; female n= 33
aged 35-70 years
NSW – Australia

-Plasma chol. > 6 mmol/L
-Plasma triacylglycerol > 1.5 mmol/L

Exclusion criteria
-No previous CVD
-No DB / chr. infl. disease
-No hypertension (< 140/95 mmHg)
-No liver or renal disease
-No anti.infl. or hypolipidemic drugs
-Not consuming sterol-enriched food or fish oil supplements
-No more than 2 fatty fish meals/week

SO n= 15	FO n= 15	SOP n= 15	FOP n= 15
Sunola oil 4 g	Tuna oil 4 g	Sunola oil 4 g Plant sterols 2g	Tuna oil 4 g Plant sterols 2g
Placebo	***n-3 PUFA***	***Sterols***	***n-3 PUFA+Sterols***

** Careful compliance controls: tracking all materials + plasma FA composition analyses*

Synergistic effects on key biomarkers

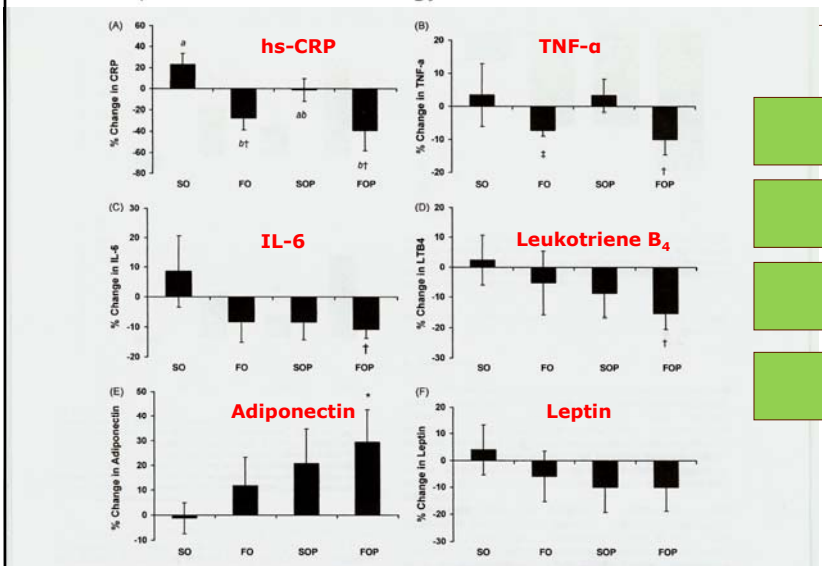


Fig. 1. Effect of dietary intervention with 4 g sunola oil/d (SO), 4 g fish oil/d (FO), SO and 2 g plant sterols/d (SOP), or FO and 2 g plant sterols/d (FOP) on selected inflammatory markers; (A) CRP, (B) TNF-α, (C) IL-6, (D) LTB_4, (E) adiponectin, and (F) leptin. Bars represent percentage change from baseline (means ± S.E.M.), following 3 weeks of dietary supplementation. Statistical analyses were performed using paired samples *t*-test: *$P<0.05$, †$P<0.01$, ‡$P<0.001$ vs. baseline. Between-group differences were analysed using two-way ANOVA. Where significance was found, Tukey's HSD post hoc analysis was used for multiple comparisons. Bars without a common letter differ, $P<0.05$.

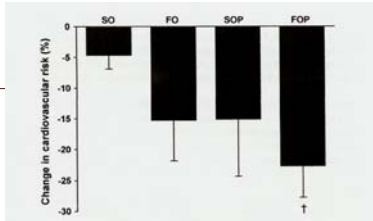
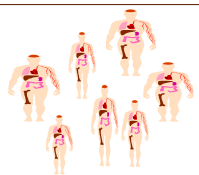


Fig. 3. Effect of dietary intervention with 4 g sunola oil/d (SO), 4 g fish oil/d (FO), SO and 2 g plant sterols/d (SOP), or FO and 2 g plant sterols/d (FOP) on cardiovascular risk. Bars represent percentage change from baseline (means ± S.E.M.), following 3 weeks of dietary supplementation. Statistical analyses were performed using paired samples *t*-test: *$P<0.05$, †$P<0.01$, ‡$P<0.001$ vs. baseline.



SUMMARY:

- High-sensitivity C-reactive protein (hs-CRP)..... ↓ **39 %** (*P*=0.009)
- Tumor necrosis factor-α (TNF-α) ..... ↓ **10 %** (*P*=0.02)
- Interleukin-6 (IL-6)..... ↓ **11 %** (*P*=0.009)
- Leukotriene B_4 (LTB_4)..... ↓ **30 %** (*P*=0.01)
- Adiponectin..... ↑ **30 %** (*P*=0.05)

Micallef & Garg 2009 Atherosclerosis 204: 476-82

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Clinical efficacy a major shortcome

3-4 main categories of food bioactives known to have health-promoting (and disease prevention) functionalities, BUT.....

Probiotics & Prebiotics	***(Fermented) Milk Peptides***	***Resveratrol a.o. Plant Phenolics***
➢ GI stability	➢ Anti-hypertensive	➢ Anti-oxidant
➢ Inflammatory gut diseases	➢ Anti-arrhythmic	➢ Anti-inflammatory
➢ Anti-inflammatory	➢ Anti-cholesterolaemic	➢ Anti-diabetic
➢ Anti-infective	➢ Anti-atherosclerotic	➢ Anti-obesigenic
➢ Immune stimulating	➢ Anti-inflammatory	➢ Liver protecting
➢ Anti-allergic	➢ Satiating (anti-obesigenic)	➢ Energy (endurance)
➢ Satiating /anti-obesigenic)		➢ Anti-carcinogenic

COMMON FEATURES: small, additive, multiple/multifactorial effects
COMMON CHALLENGE: impressive laboratory and pre-clinical data – BUT human clinical trials often inconclusive

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Food and health: the functional paradox

'…ds'

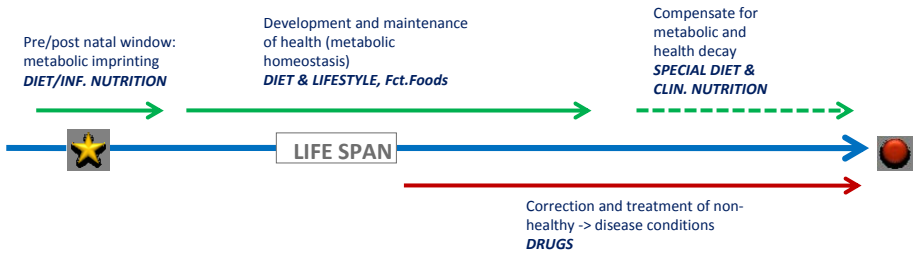
➢In regulatory terms, functional foods is not a legal category
➢Directive on Nutrition Profiles and Health Claims apply to all…

…AND BENEFICIAL FOR YOU AND ME

ActiFoods

Example of PPP needs and potentials

The framework of personalized/public Health & Nutrition – a societal issue (private & public)



…which needs substantial new scientific developments and understanding:

- ***nutritional/physiological 'omics***
- ***role(s) of metabolic stress***
- ***measures (markers) of health***

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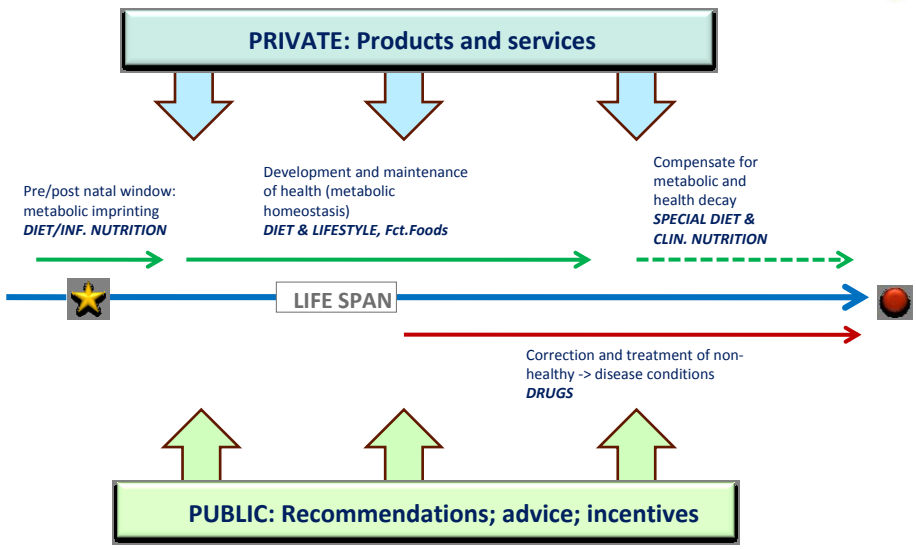
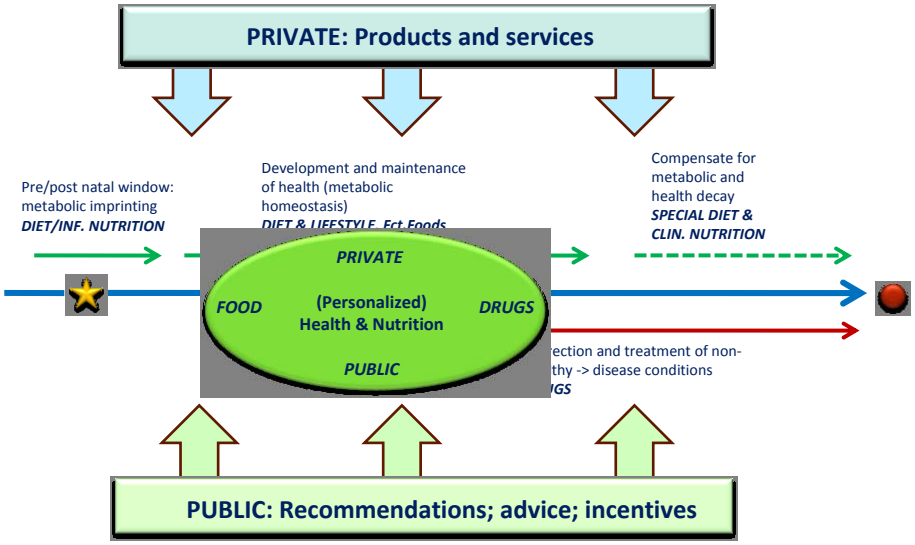
Example of PPP needs and potentials



Example of PPP needs and potentials



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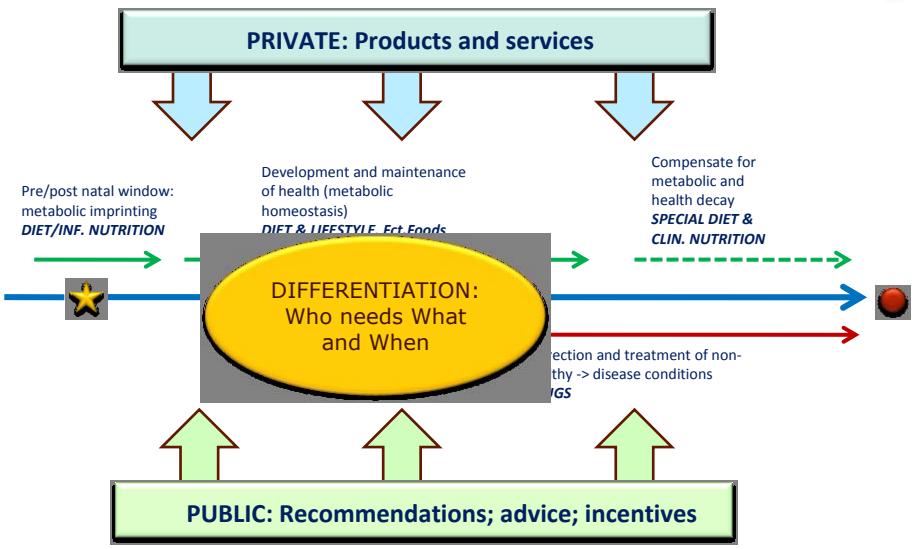
Example of PPP needs and potentials



Commercial value of the nutritype concept

FOOD	FCT. FOOD	NUTRITYPE FOOD	FOOD SUPL.	FOOD SUPL.+
Food w. intrinsic health fct.	Food w. added health fct.	Health fct. especially for you…	Health fct. without food	Health fct. especially for you…

Mass marketing → **Differential & personalized**

Added value, product differentiation and personalization will go hand-in-hand in the Food and Nutrition industry

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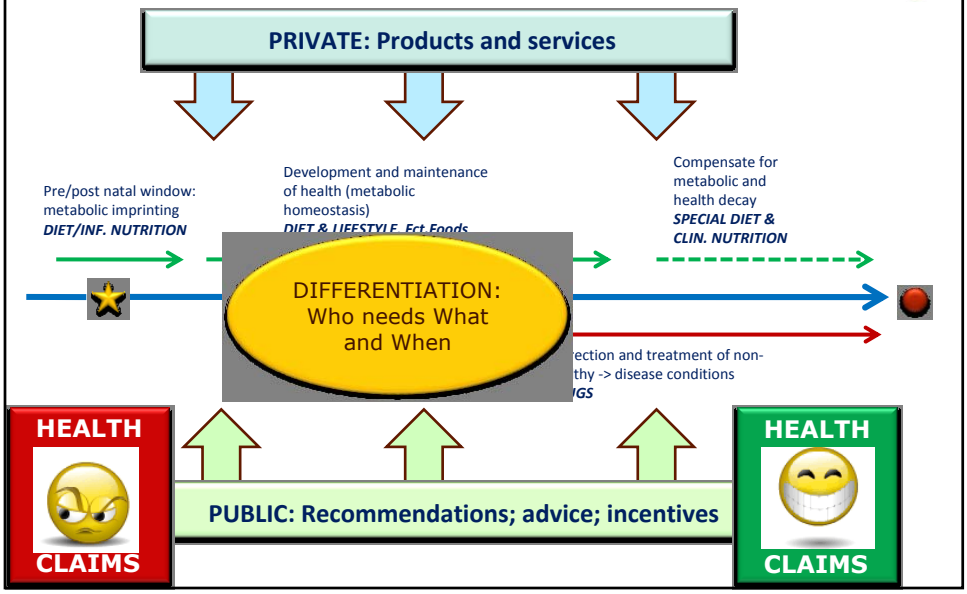
Mass marketing → Differential & personalized

Added value, product differentiation and personalization will go hand-in-hand in the Food and Nutrition industry

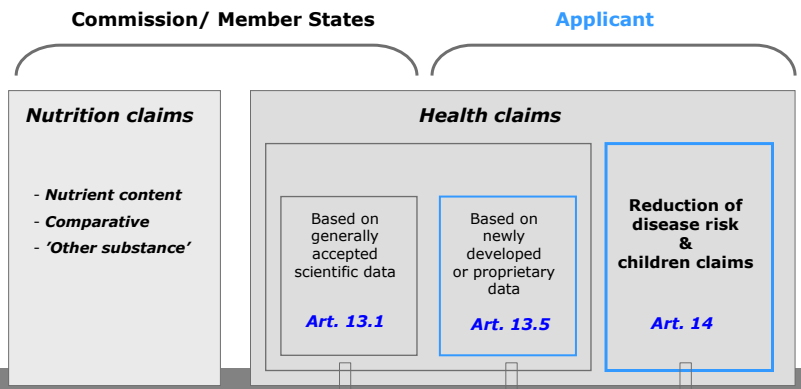
- Nutritype definitions will be a major knowledge base for the industry in order to embark on NPD in the move from mass marketing towards personalized nurition
- - which they otherwise would be resistant to due to the 'unsurmountable' task of moving directly to individualized products with no fit to existing business models

Example of PPP needs and potentials



EU health claims: classification and burden of proof

"Regulation (EC) No 1924/2006 on Nutrition and Health Claims made on food"



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EFSA Evaluation: Criteria for Substantiation (1/2)

- **Characterisation of food/constituent**
  - Is it measurable? Can it be verified by regulators?
  - Is it the one for which the scientific evidence is based?
- **Is the claimed effect beneficial to human health?**
  - Validity of endpoint, size of effect, benefit in EU population groups
- **Causality of the relationship**
  - Is a cause and effect relationship established between the consumption of the food and the claimed effect in humans?
  - Strength, consistency, specificity, dose-response, biological plausibility

Courtecy of Dr. Inge Tetens, NDA-EFSA

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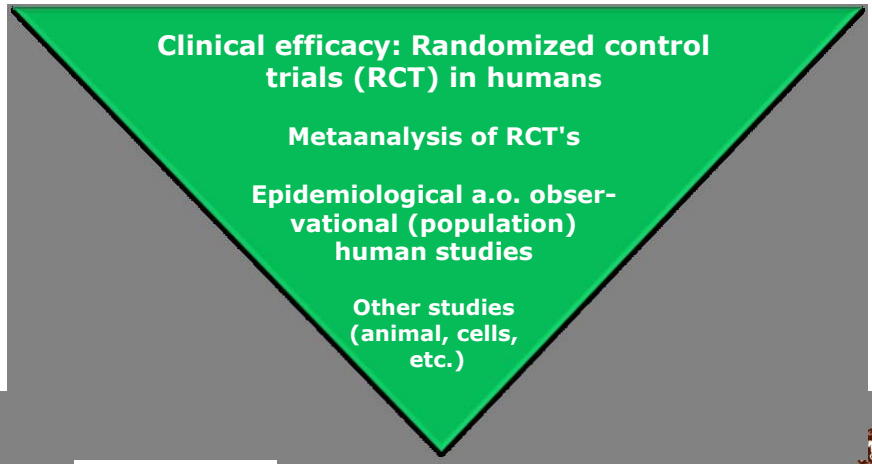
EFSA Evaluation: Criteria for Substantiation (2/2)

- **Food quantity required for the claimed effect**
  - Is the quantity of food/constituent proposed for the claimed effect adequate?
  - Quantity and pattern of consumption to obtain the claimed effect?
- **Representativeness of data for target population**
  - Is the specific study group(s) in which the evidence was obtained representative of the target population for which the claim is intended?
  - Patients vs healthy subjects; adults vs children?
- **If a cause and effect relationship is established, then state conditions and restrictions of use**

Courtecy of Dr. Inge Tetens, NDA-EFSA

Scientific Substantiation Hierarchy: 'Clinical Dogma'



EU health claims: classification and burden of proof

"Regulation (EC) No 1924/2006 on Nutrition and Health Claims made on food"

Commission/ Member States | **Applicant**

Nutrition claims

- ***Nutrient content***
- ***Comparative***
- ***'Other substance'***

Health claims

Based on generally accepted scientific data

Based on newly developed

Reduction of disease risk & children claims

'GOLDEN STANDARD'

-is still the linear clinical documentation approach

(pharma legacy, wide acceptance)

Positive list

'Fast track' EFSA Procedure

Committee EFSA Procedure

ActiFoods

EFSA evaluation – First batch Art. 13 claims

- First batch of 94 EFSA opinions on 523 Art. 13 claims (out of total 4185) published October 1, 2009
- Includes claims on:
  - vitamins
  - minerals
  - dietary fibres
  - fatty acids
  - probiotic bacteria
  - other (sugar-free chewing gum, plant extracts etc.
- **1/3 positive** opinions, mostly on vitamins and minerals
- **2/3 negative** opinions, mostly on probiotic bacteria (all negative), plant extracts, other
- Two key justifications for negative opinions
  1) weak scientific evidence
  2) substance not sufficiently characterised (not well identified

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Examples of recent EFSA opinions - published adoptions

Art. 14 June 2009	❑ Plant stanols and plant sterols and blood LDL-cholesterol - scientific opinion on foods suitable for use of claim
Art. 14 July 2009	❑ Danacol® and lowering/reducing blood cholesterol - low fat fermented milk - scientific substantiation of health claim related to reduced risk of (coronary) heart disease
Art. 14 July 2009	❑ Calcium + Vitamin D3 chewing tablets and bone loss - scientific substantiation of health claim related to reduced risk of osteoporotic fractures
Art. 14 Jan. 2009	❑ Kinder Chocolate® and child growth - scientific substantiation of health claim related to product 'helps to grow'
Art. 13.5 July 2009	❑ Regulat® and immune system: *Lactobacilli* fermented vegetable/fruit extract - scientific substantiation of health claim related to enhancement/modulation/improvement/regulation of the immune system
Art. 13.5 May 2009	❑ Natural Push-Up® tablets and capsules (hops) and female breast-enhancement - scientific substantiation of health claim related to 'firmer and fuller breasts'

To date (02-11-2009) the NDA panel has received 260 Article 14 applications
- 21 applications withdrawn
- 55 scientific opinions have been adopted,
- covering 62 applications

COMMISSION REGULATION (EC) No 983/2009
0f 21 October 2009

on the authorisation and refusal of authorisation of certain health claims made on food and referring to the reduction of disease risk and to children's development and health (Article 14)

efsa
European Food Safety Authority

Based upon earlier Scientific Opinions from EFSA:

6 opinions related to applications for reduction of disease risk claims ~ Art. 14 (1)(a)

17 opinions related to applications for health claims referring to children's development and health ~ Art. 14 (1)(b)

NB! This is now European Law, harmonised for implementation in Member States

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'***Plant sterols*** have been proven to lower/reduce blood cholesterol significantly. Blood cholesterol lowering has been proven to reduce the risk of (coronary) heart disease'
- Unilever PLC & Unilever NV -

'By actively lowering/reducing LDL-cholesterol (by up to 14% within 2 weeks, by blocking cholesterol absorption), ***plant stanol esters*** reduce the risk of (coronary) heart disease'
- McNeil Nutritionals / Benecol -

'Regular consumption of essential fatty acids is important for proper growth and development of children'
- health claim on ***α*-linolenic acid (ALA) and linoleic acid (LA)**
- Unilever PLC & Unilever NV -

1) '***Vitamin D*** is essential for the bone growth of children'

2) '***Calcium*** is needed for the healthy bone growth of children'

3) '***Calcium and vitamin D***, as part of a healthy diet and lifestyle, build stronger bones in children and adolescents'
- 1-2: Association de la Transformation Laitière Francaise (ATLA) and 3: Yoplait Dairy Crest Ltd. -

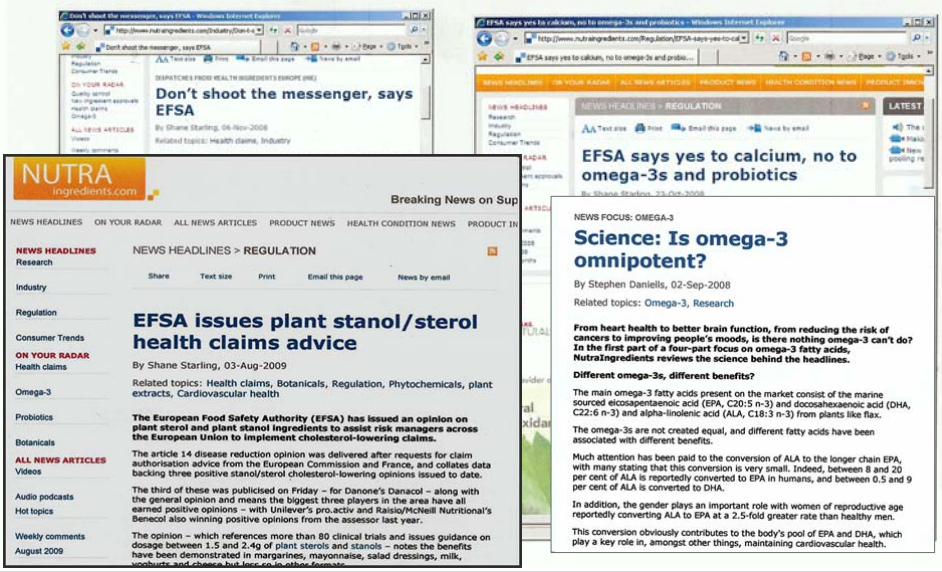
'***Proteins of animal origin*** contribute to children's bone growth'
- Association de la Transformation Laitière Francaise (ATLA) -

Authorised health claims – EC No 983/2009

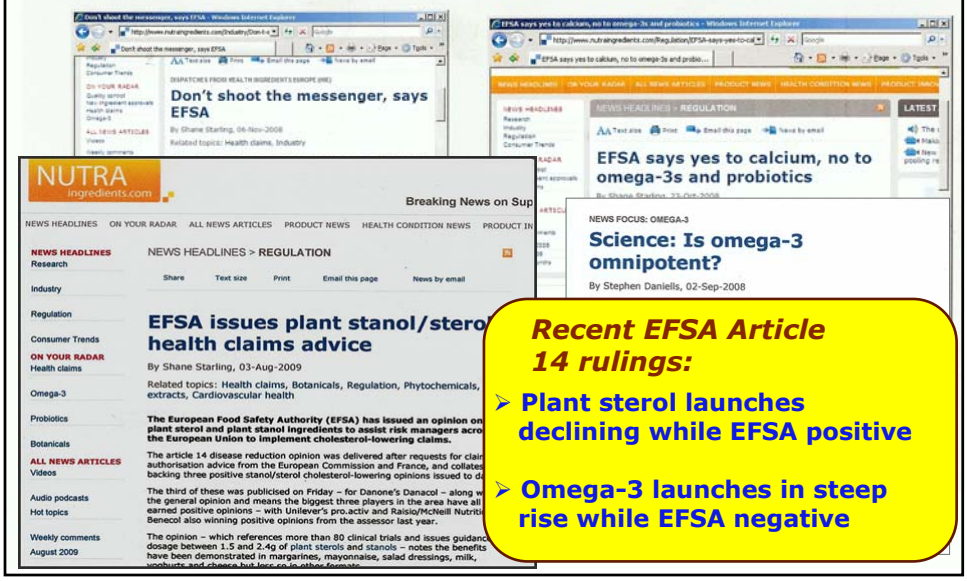
NeOpuntia® and cardiovascular risks (esp. HDL cholesterol)
Evolus® low-fat fermented milk and arterial stiffness
Docosahexaenoic acid (DHA) and arachidonic acid (ARA) and neuronal development of the brain and eyes -*
Dairy foods (milk and cheese) and dental health in children
Dairy foods and a healthy body weight
Regulat®.pro.kid IMMUN / ***Regulat®.pro.kid BRAIN*** and immune system / mental & cognitive development in children
I omega kids®/Pufan 3 kids® and 'calming', 'serenity and beneficial development of the child', 'help to support vision', 'help to support mental development', 'help to promote concentration', 'helps to promote the thinking capacity', 'help to support the learning ability'

Refusal of authorisation of health claims – EC No 983/2009:
→ products with these claims must be withdrawn from market at the latest 6 months after this adoption

EFSA rulings debated…



… and not in synch with product introductions

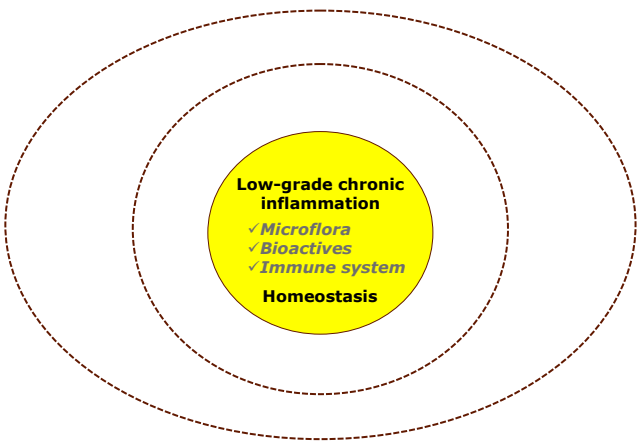


Recent EFSA Article 14 rulings:

- **Plant sterol launches declining while EFSA positive**
- **Omega-3 launches in steep rise while EFSA negative**

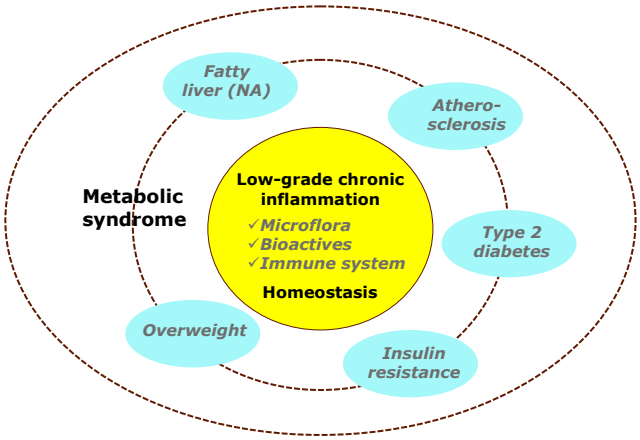
Documentation: cause – effect - efficacy

The biomarker challenge



Documentation: cause – effect - efficacy

The biomarker challenge



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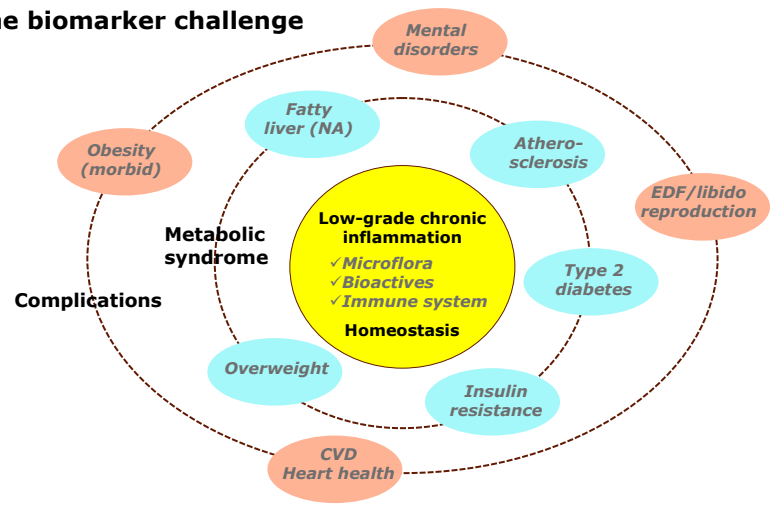
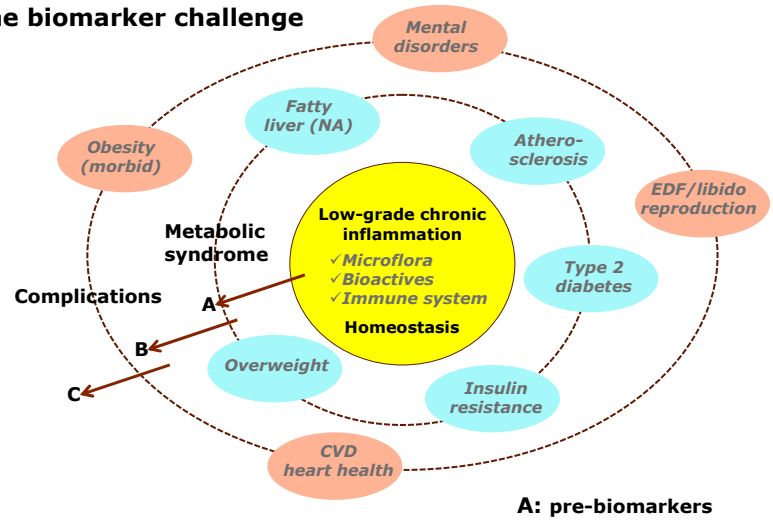
Documentation: cause – effect - efficacy

The biomarker challenge



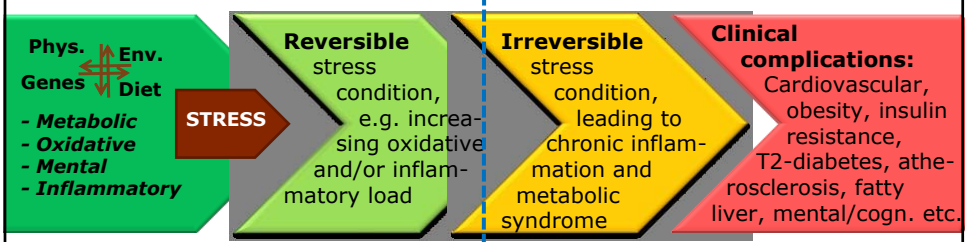
Documentation: cause – effect - efficacy

The biomarker challenge



A: pre-biomarkers
B: surrogate endpoints (validated)
C: endpoints (clinical)

HEALTH = not just the 'absence of disease', but the organism's ability to maintain metabolic homeostasis (balance)



RESEARCH DIRECTION: Under experimental conditions, use weak stress challenges and investigate the effect of ingested health compounds (plant/food bioactives) to revert to homeostatic healthy condition. Parallel omics analyses (transcriptomics / proteomics / metabolomics) may confirm which genes / pathways / compounds are involved in ***maintenance of health***…→ **biomarkers of health**

OG HUSK:

Sundhed/forebyggelse og medicin er helt forskellige mht. formål, produkter, godkendelseskrav, forretningsmodeller osv…

Illustreret Videnskab 13 (2009), 24-31

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OG HUSK:

Sundhed/forebyggelse og medicin er helt forskellige mht. formål, produkter, godkendelseskrav, forretningsmodeller osv…

-MEN GLEM IKKE:

At bioaktive stoffer i fødevarer sandsynligvis er involveret i en række tilfælde af fødevarer-medicin interaktioner, positive←→ negative?

Illustreret Videnskab 13 (2009), 24-31

CONCLUSIONS

- Framework for food bioactives is that all food is functional, due to the content of bioactives – with positive and negative effects, different for each individual – with a potential for identification of nutritypes (groups).

- Health is not just 'absence of disease' but the organism's ability to maintain metabolic homeostasis (balance) and counteract reversible stress conditions.

- From a user-driven view (consumer's and society's needs) there are huge potentials in the development of age- and nutritype specific food and nutrition products. This requires intensified private-public interactions, including approval and accept of well-documented health claims.

- A breakthrough in EU Regulations has recently occurred with scientific opinions (EFSA) re Article 13 and Article 14 claims applications – and first EU final approval of 6 claims and rejection of 17 claims is now law and must be implemented in Member States, incl. DK

- So far, only claims related to defined chemical entities (sterol/stanol esters, calcium and vitamin D have been approved as disease reduction claims, documented via human clinical trials. Many bioactives (probiotics, antioxidants, omega-3 PUFA's, dairy peptides etc.) still suffer from 'incompatibility' with the clinical dogma – and new ways to identify and validate biomarkers for health (not for disease) is needed

- This calls for more holistic and omics-based research directed at reversing stress impacts on health (metabolic, oxidative, inflammatory, mental etc.) via the action of bioactives in food in order to avoid progress into (irreversible) conditions leading to metabolic syndrome and associated clinical complications.

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FOOD

Tak for ordet

HEALTH