Epigenetik in der Praxis. Haben wir die Gesundheit in der eigenen Hand? Epigenetik und Salutologie

Alexander G Haslberger

Classic Bloody Mary

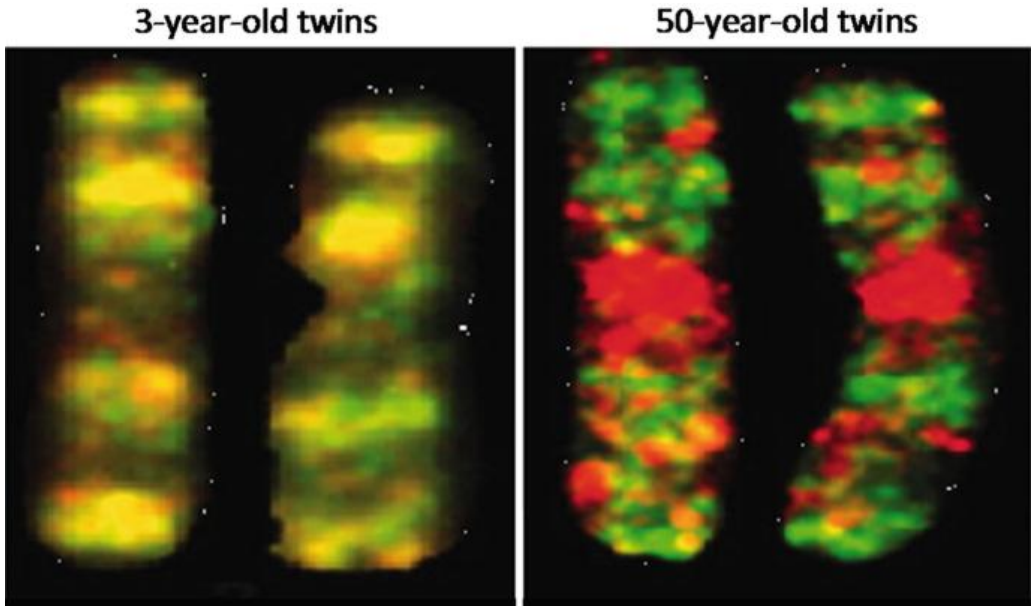
Tomatoes are a good source of various polyphenols, including:

- **Quercetin:** A flavonoid known for its antioxidant and anti-inflammatory properties.
- **Lycopene:** A carotenoid, also an antioxidant, responsible for the red color of tomatoes.
- **Other Phenolic Acids:** Tomatoes contain other phenolic acids that contribute to their overall antioxidant capacity.

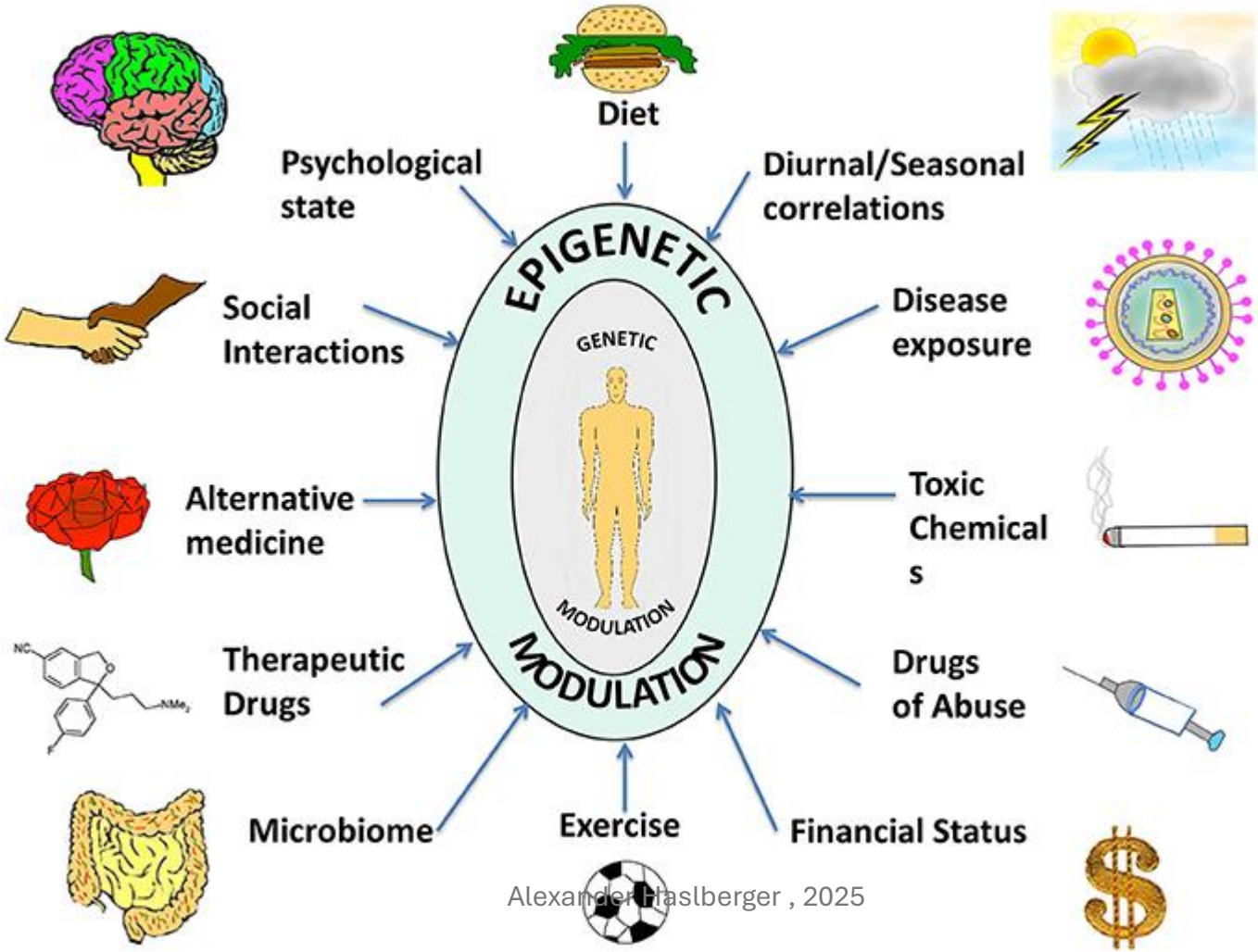
SYSTEM - BIOLOGIE
INSPIRED BY NATURE

HealthBioCare GmbH

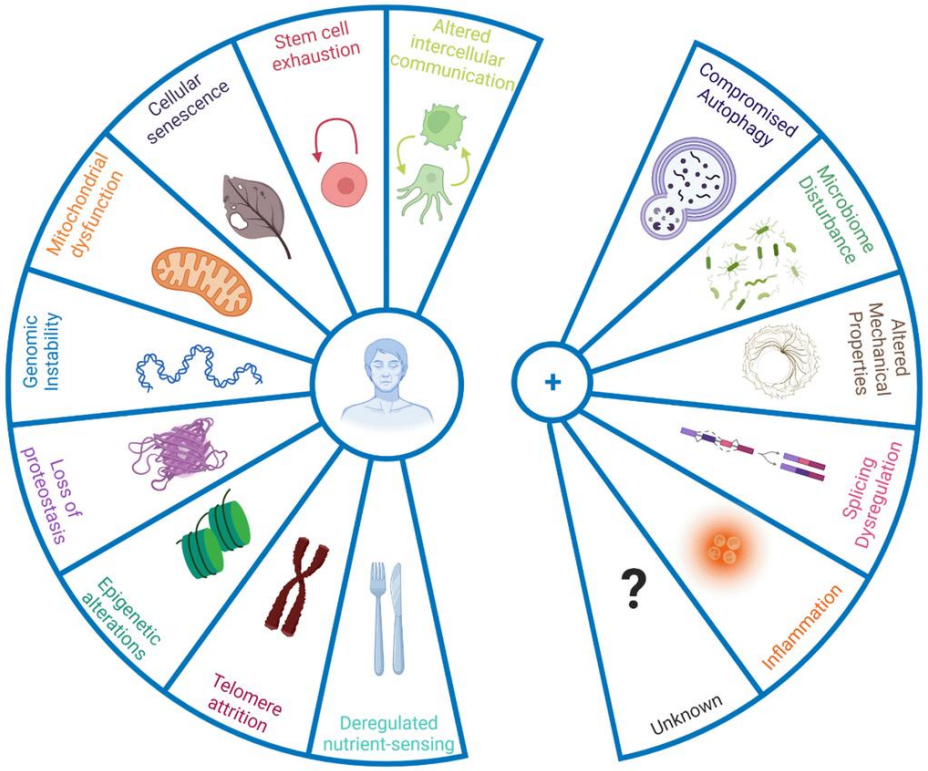
Epigenetik: Monozygote Zwillinge

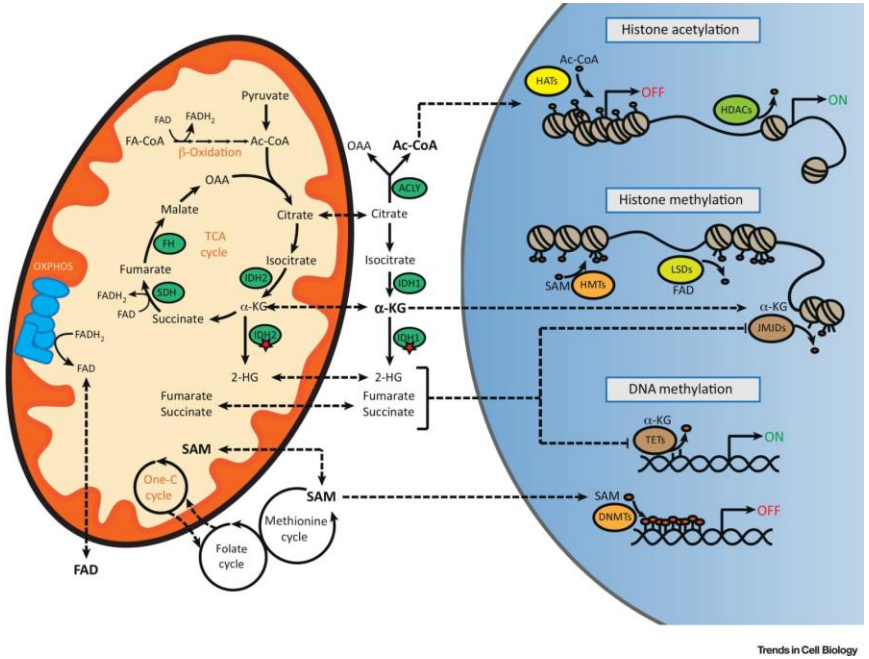


Warum Epigenetik I: Einflüsse von der Umwelt , aber reversibel

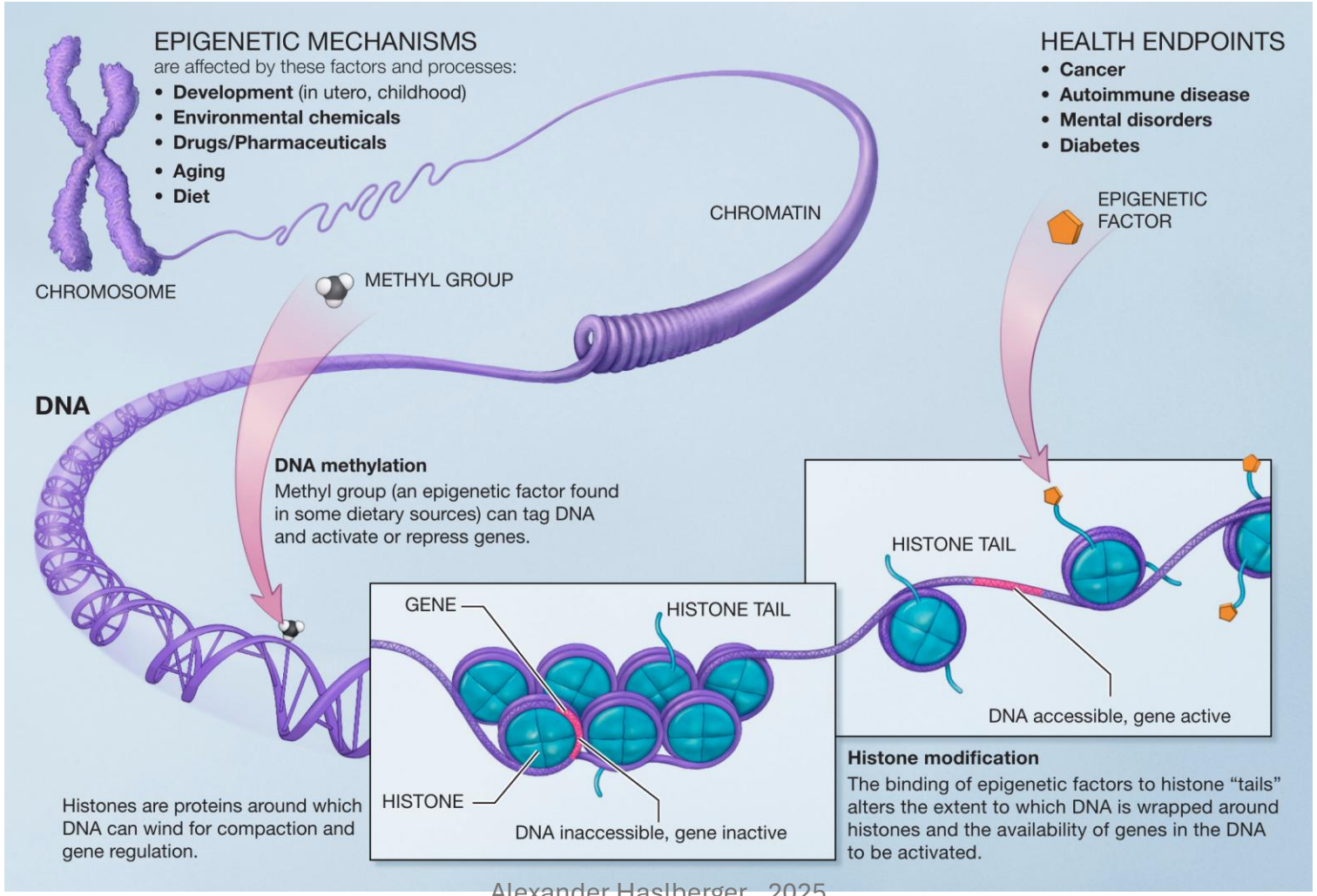


Warum Epigenetik II: Epigenetik reguliert Gene die in Alterungsprozessen beteiligt sind hallmarks fo ageing(zb Mitochondrien)

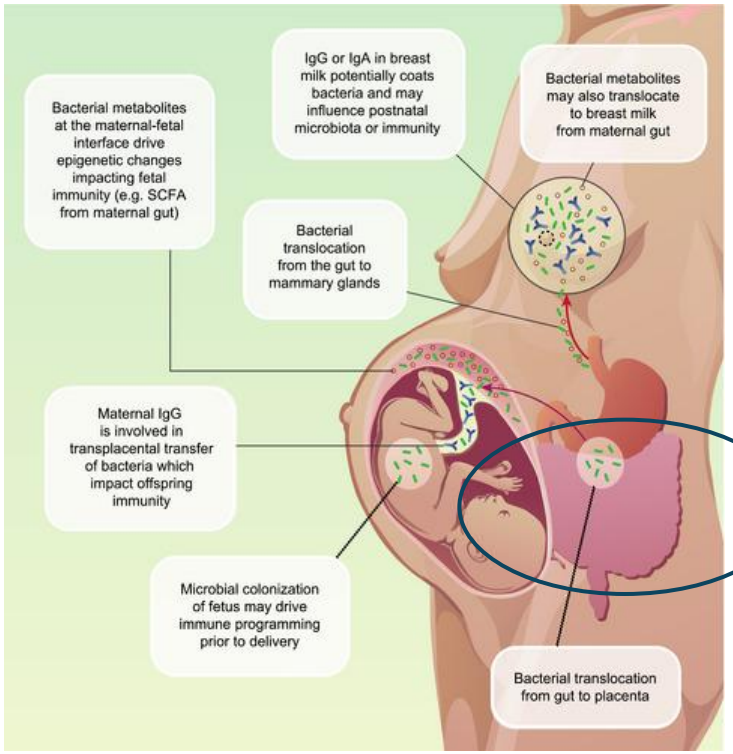


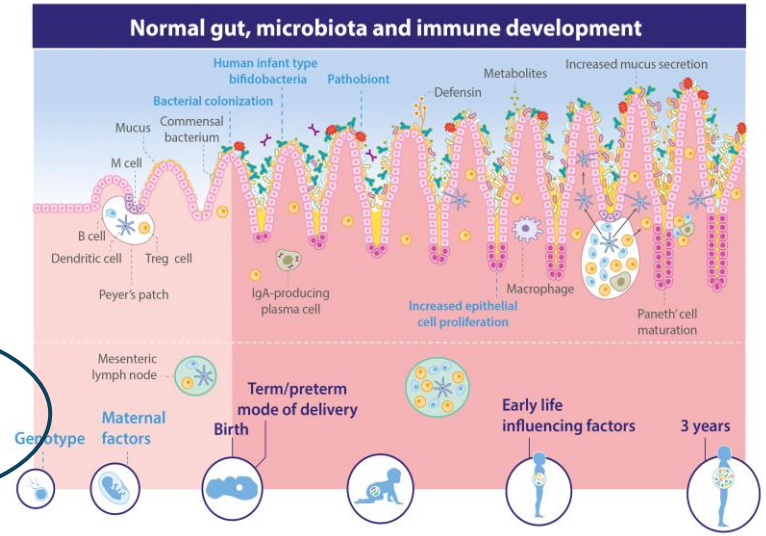


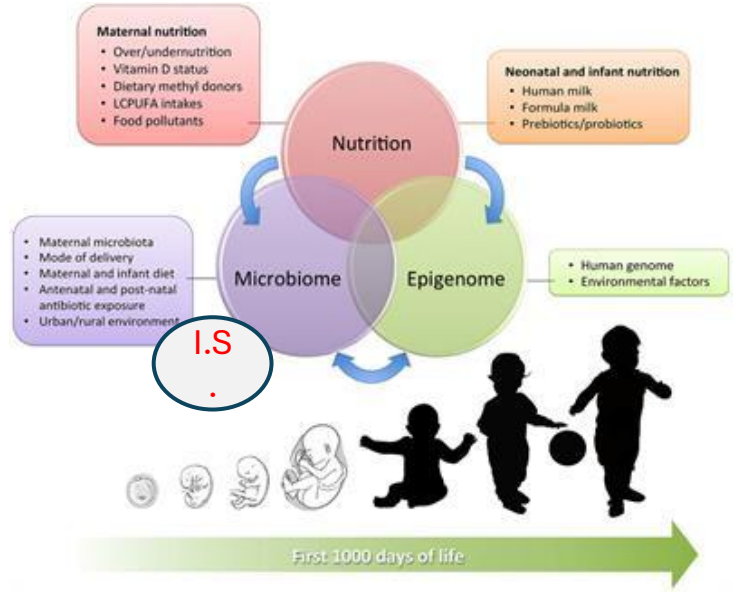
Warum Epigenetik III Mechanismsn



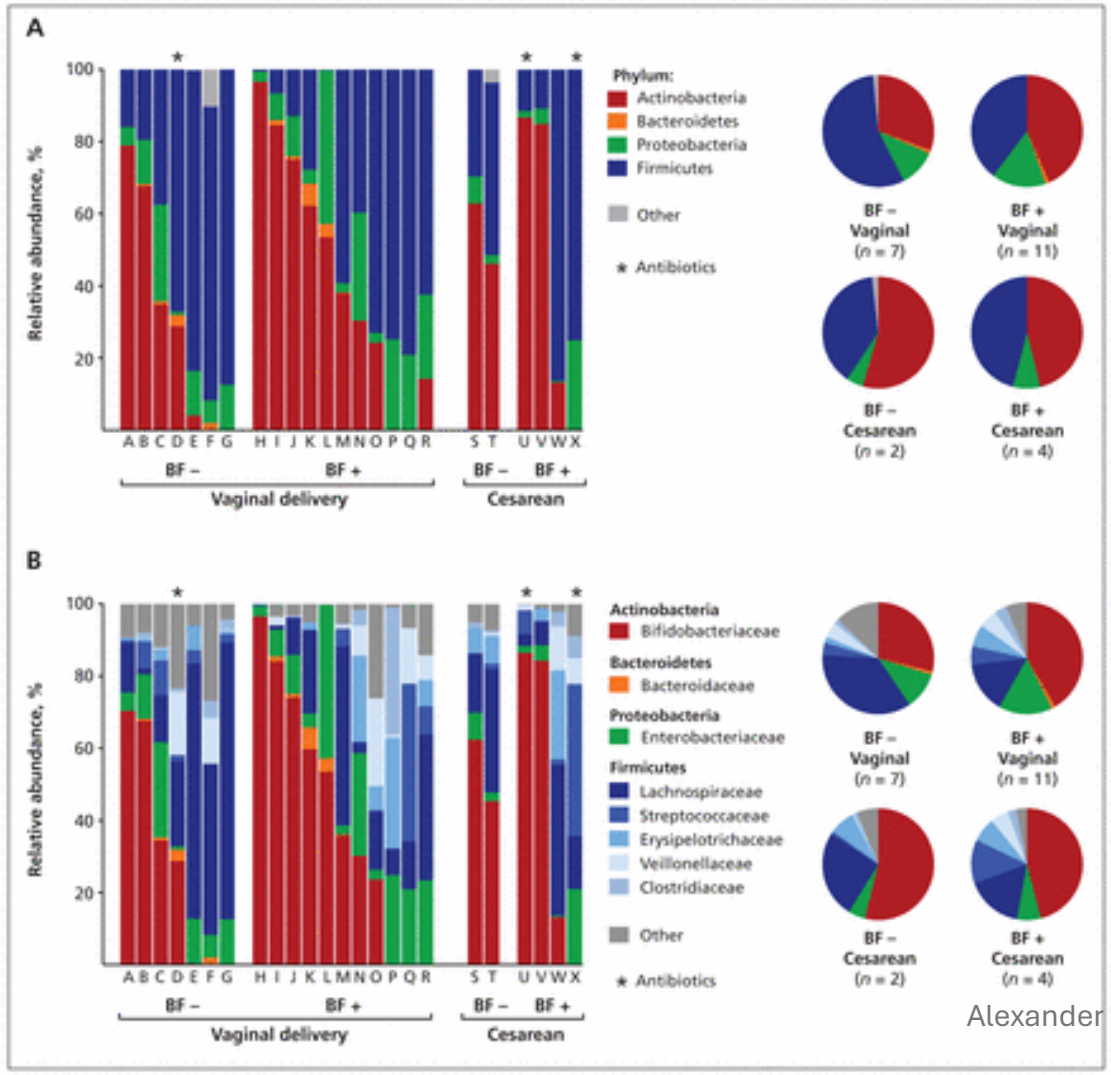
Entwicklung : Mikrobiota, Epigenetik und I.S. Interagieren. First 1000 days of life







Mikrobiota : unterschiedliche Entwicklungen, die Rolle der Diversität



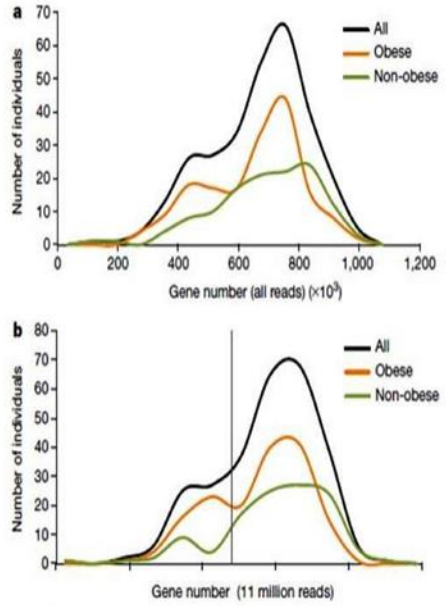
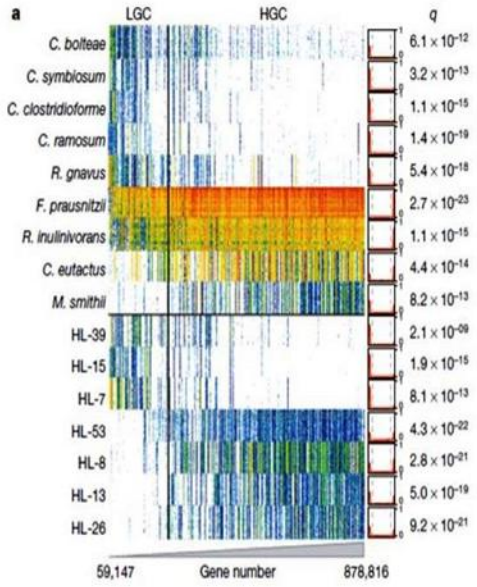
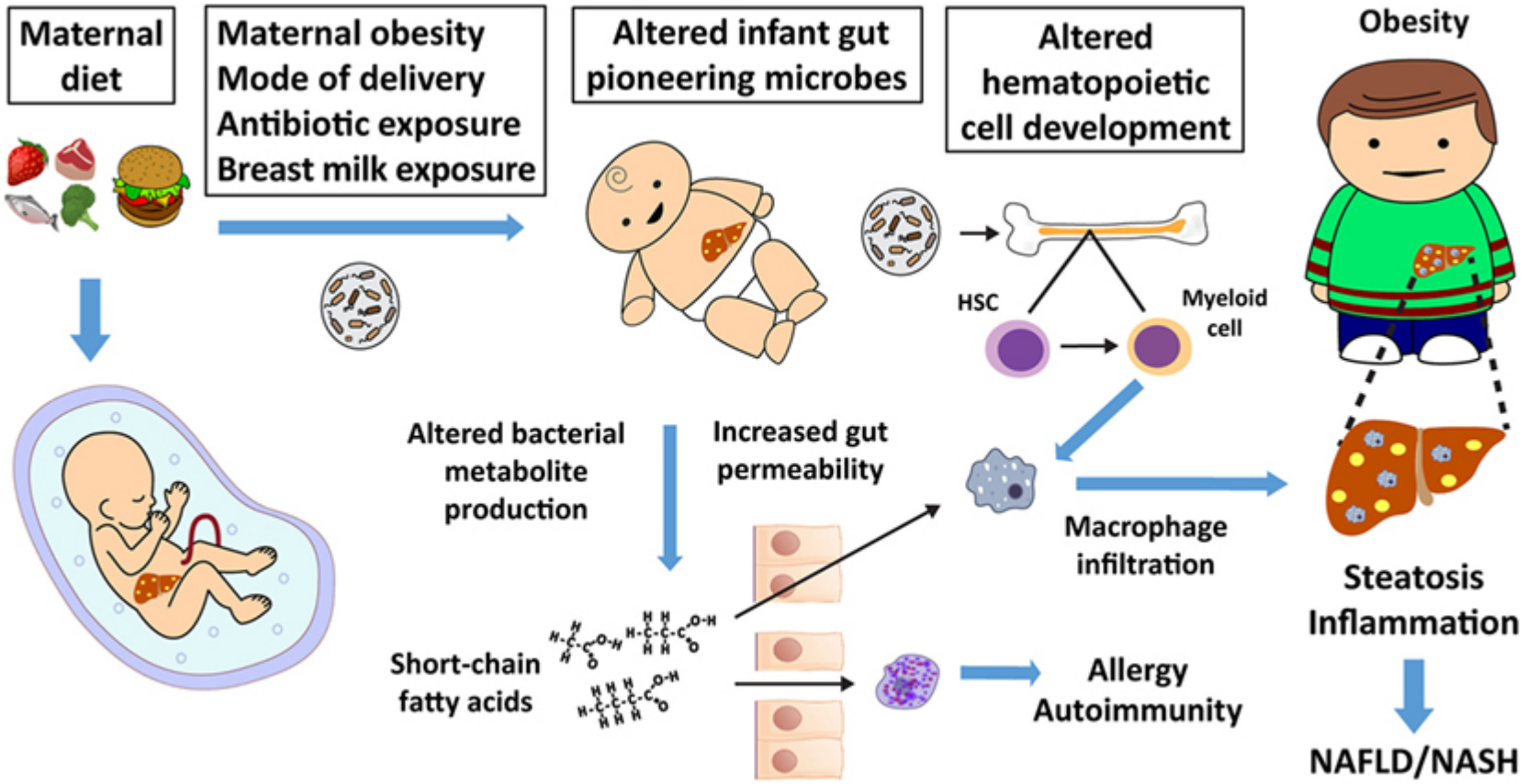


Figure 1 | Distribution of low and high gene count individuals ($n = 292$). a, Gene counts from all uniquely matched reads. b, Gene counts adjusted to 11 million uniquely mapped reads per individual. Vertical line indicates the threshold of the LGC and the HGS individuals; the observed bimodal distribution was not statistically significant by the dip-test.

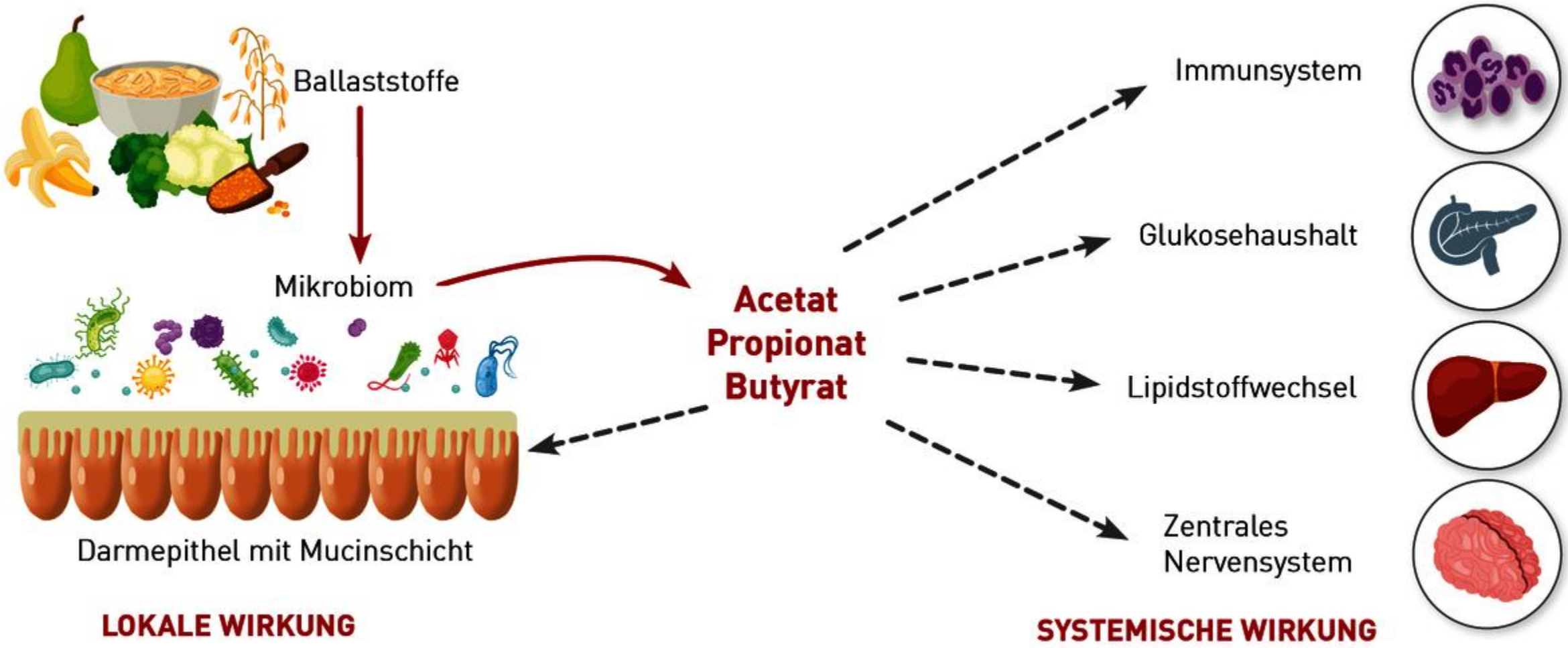


(Le Chatelier E. et al., 2013)
MetaHitConsortium

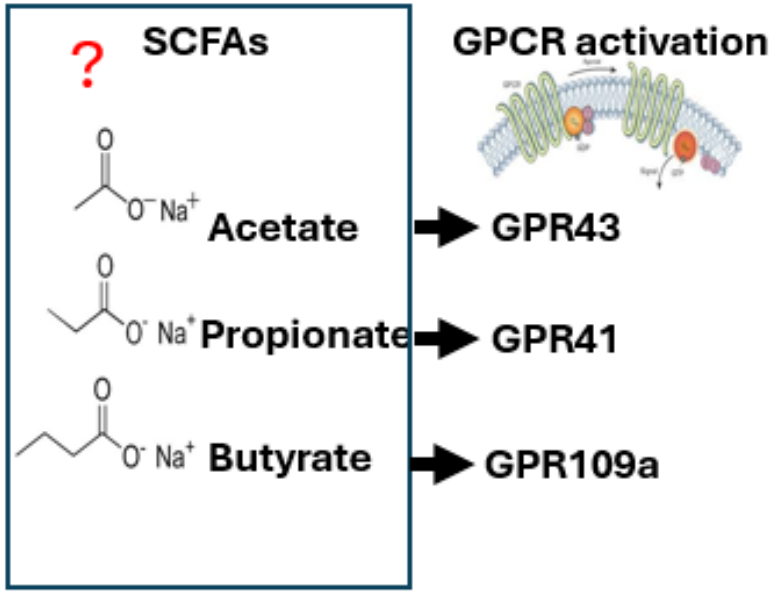
Frühe Mikroben verändern die Entwicklung des Immunsystems und die metabolische Homöostase

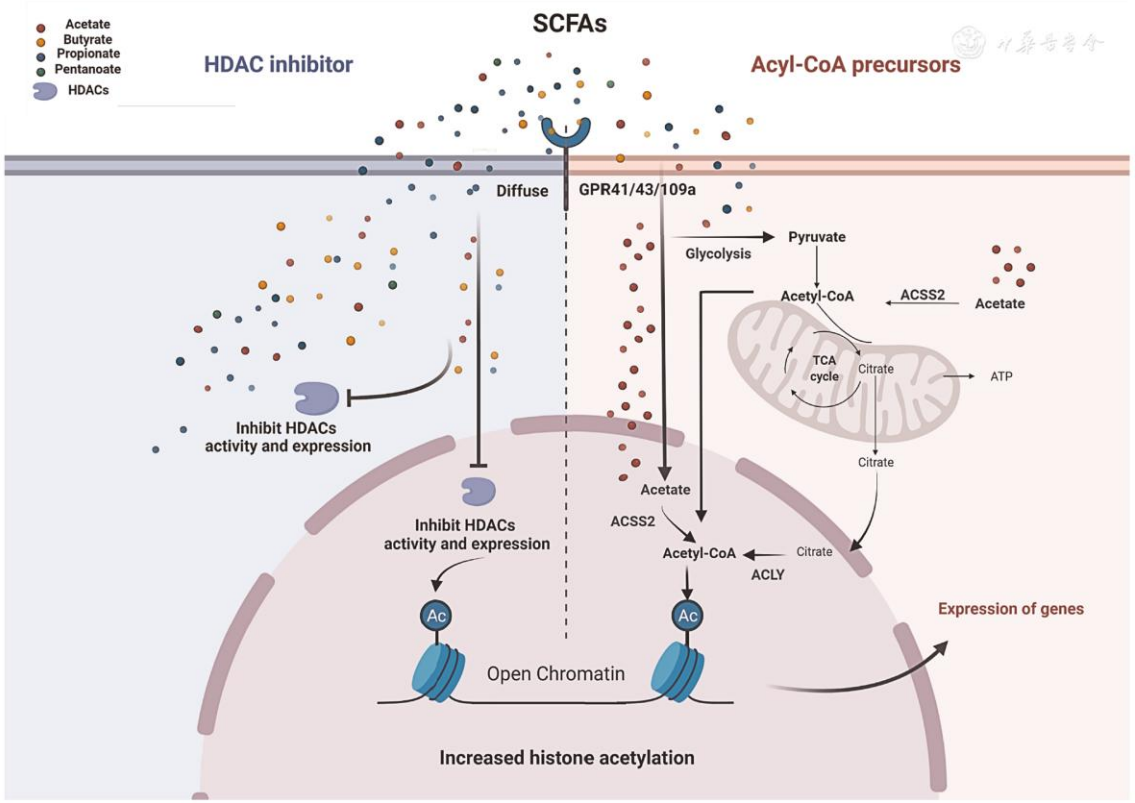


Ernährung und die Rolle von Faserstoffen



Wirkungsmechanismus von Ballaststoffen: Kurzkettige Fettsäuren (SCFAs)





Butyrat, Beta-hydroxy Butyrat(BHB), Epigenetik und Gesundheit

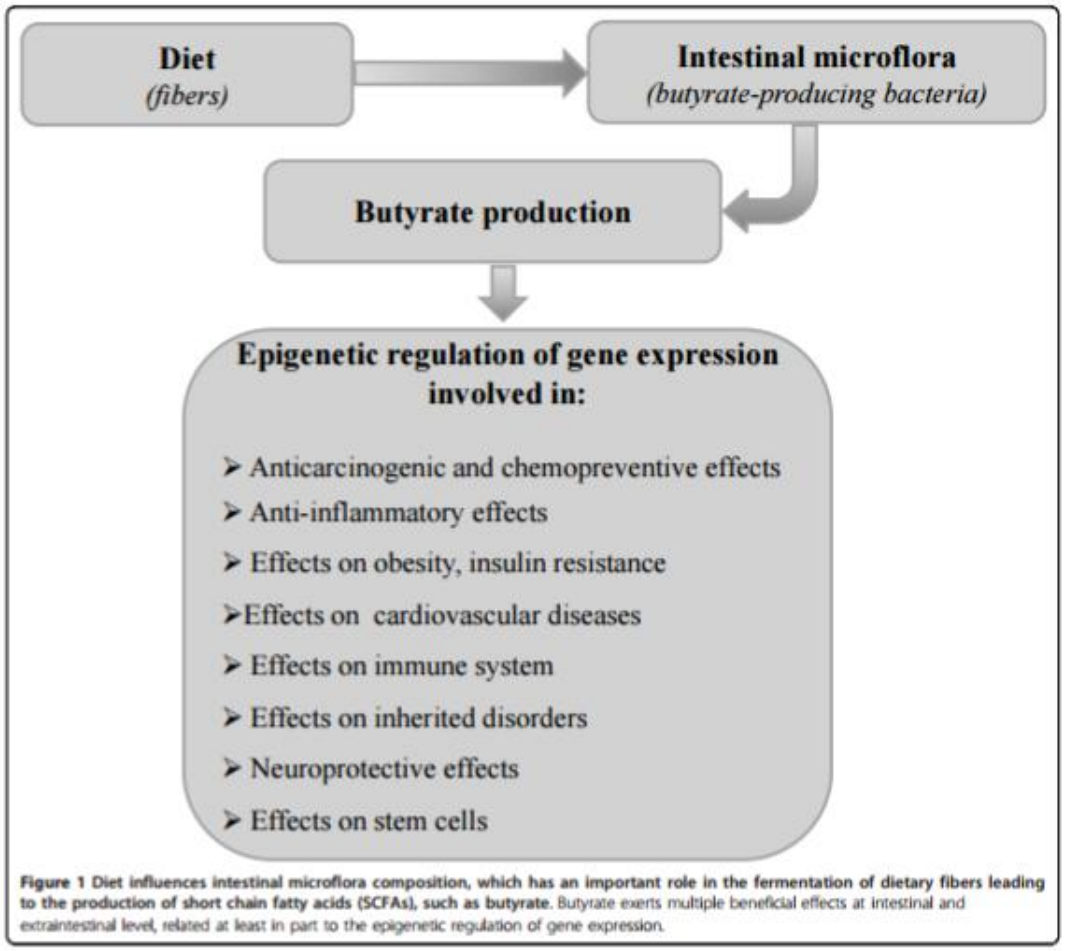
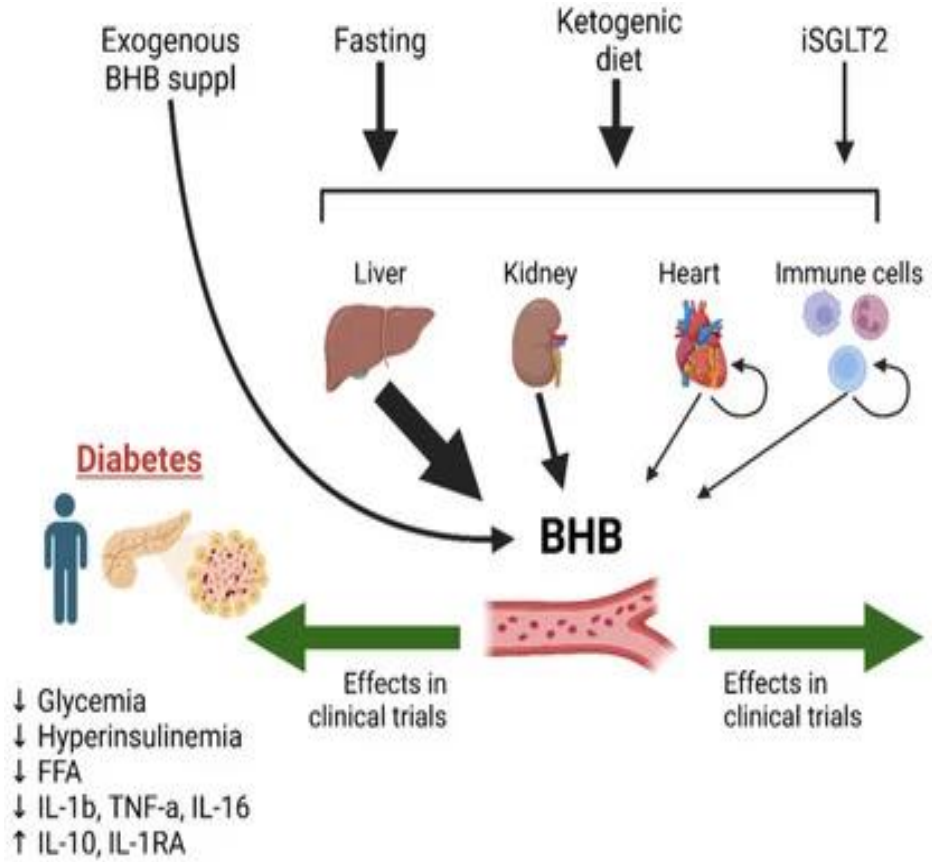
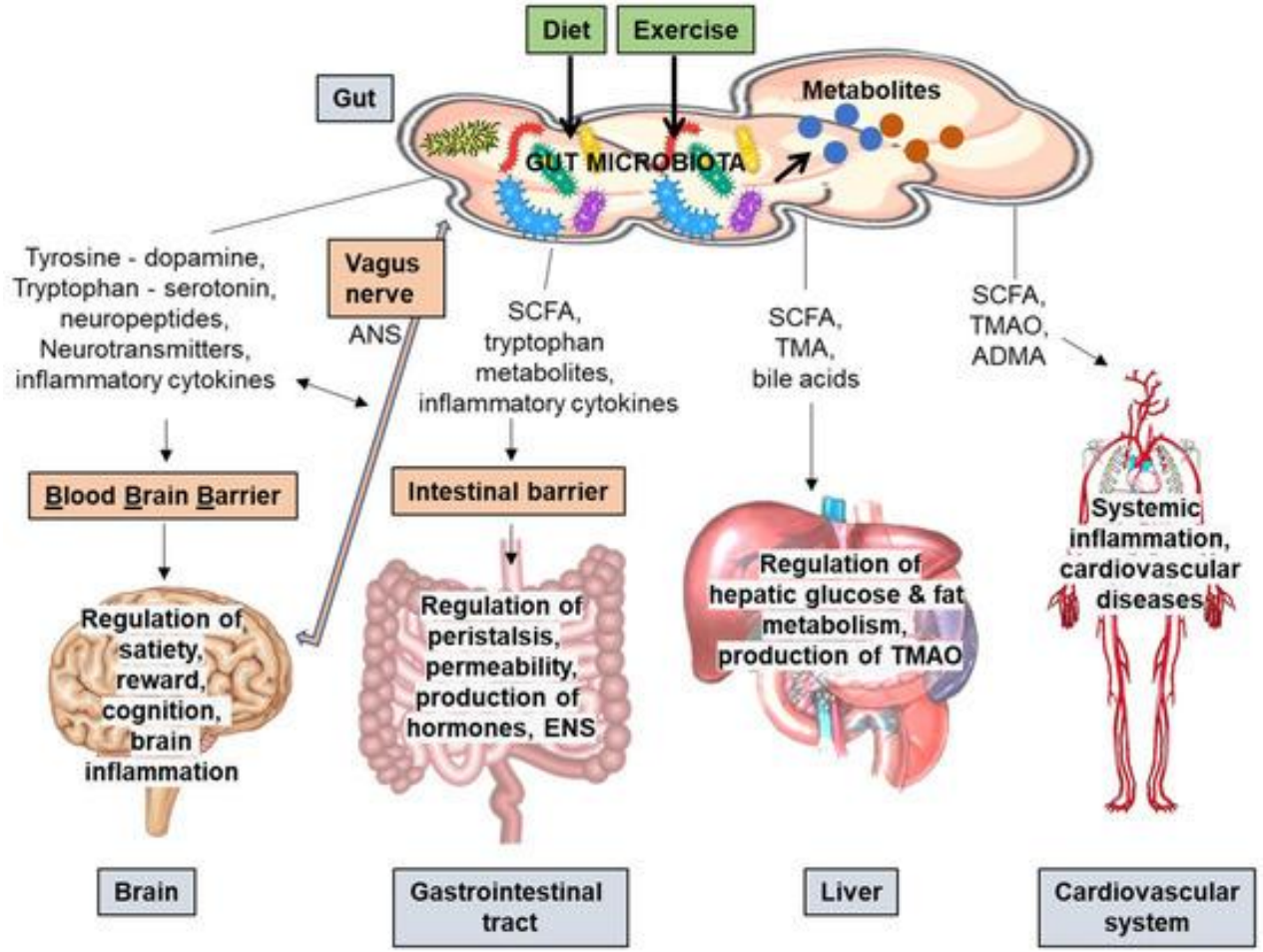


Figure 1 Diet influences intestinal microflora composition, which has an important role in the fermentation of dietary fibers leading to the production of short chain fatty acids (SCFAs), such as butyrate. Butyrate exerts multiple beneficial effects at intestinal and extraintestinal level, related at least in part to the epigenetic regulation of gene expression.

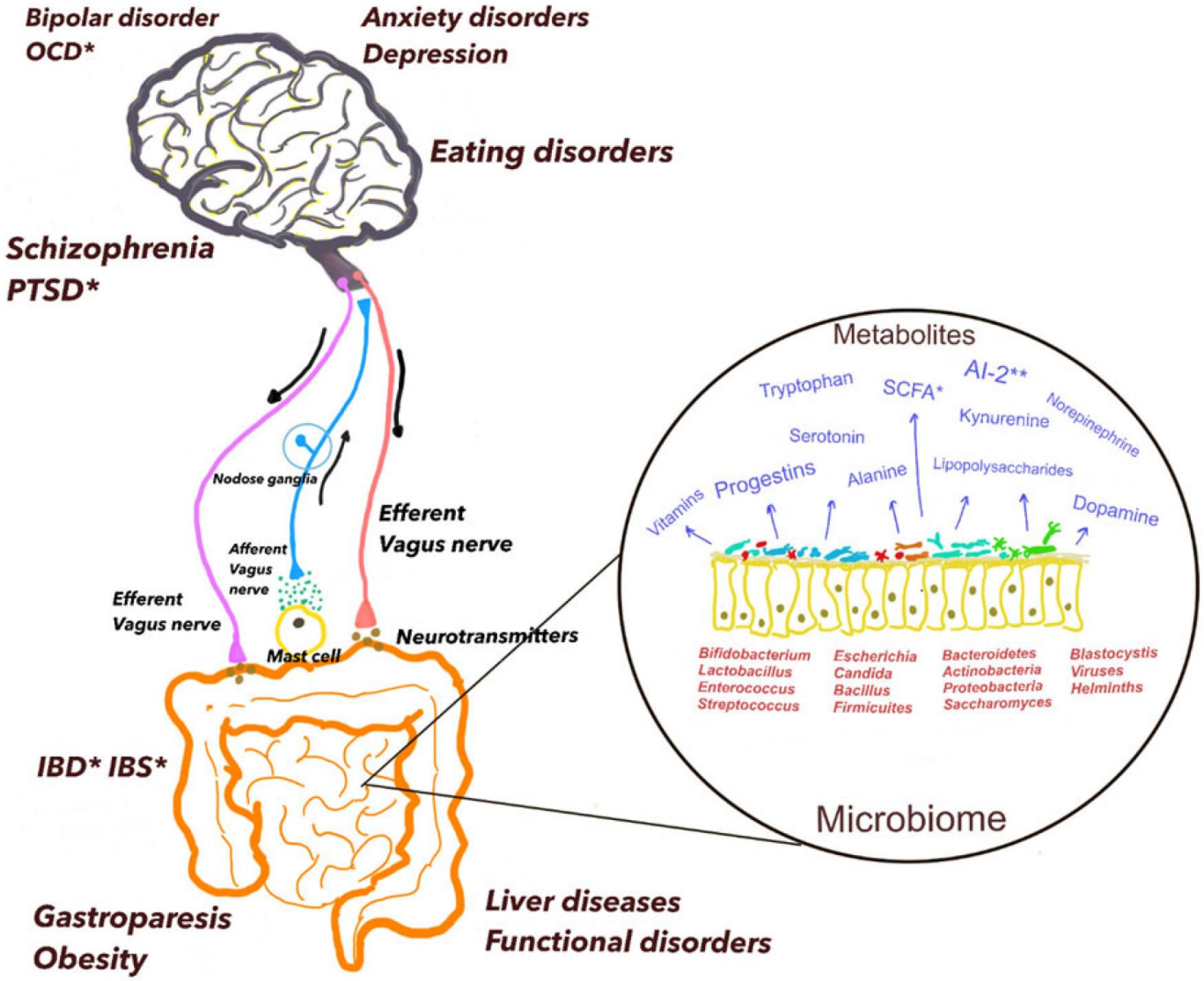


Na glucose transporter

Metabolite von Mikrobiota

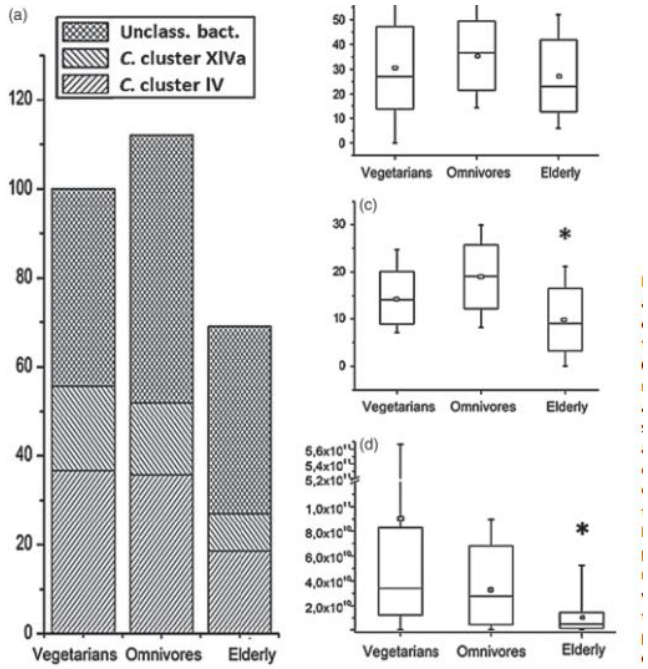


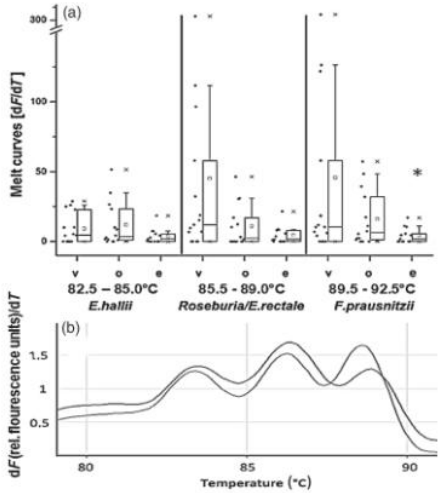
Gut-Microbiota-Brain Communication



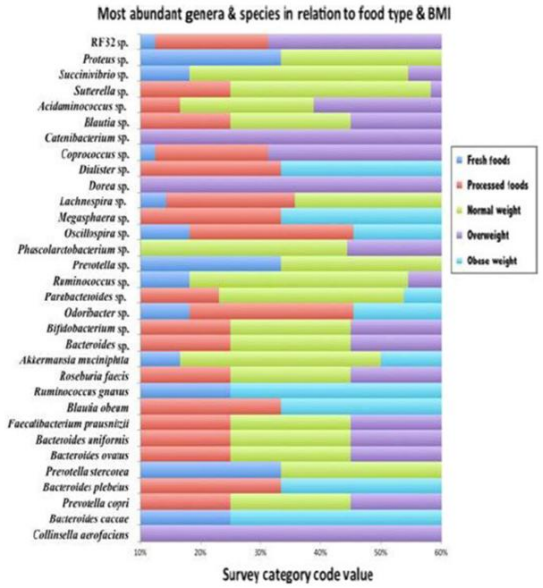
Cryan, John F., and Timothy G. Dinan. "Mind-altering microorganisms: the impact of the gut microbiota on brain and behaviour." Nature reviews neuroscience 13.10 (2012): 701-712.

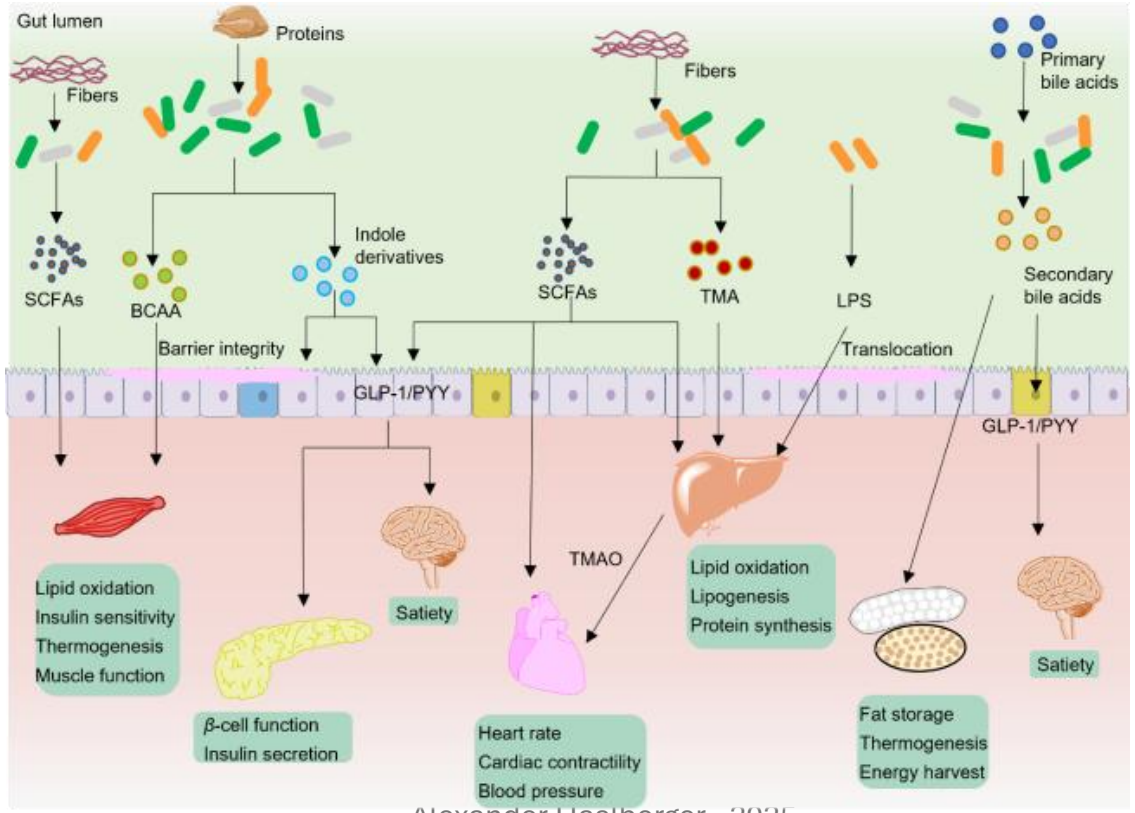
SCFAs bei älteren Menschen: Rückgang der SCFA-Produzenten und „Butyrat bei älteren Menschen

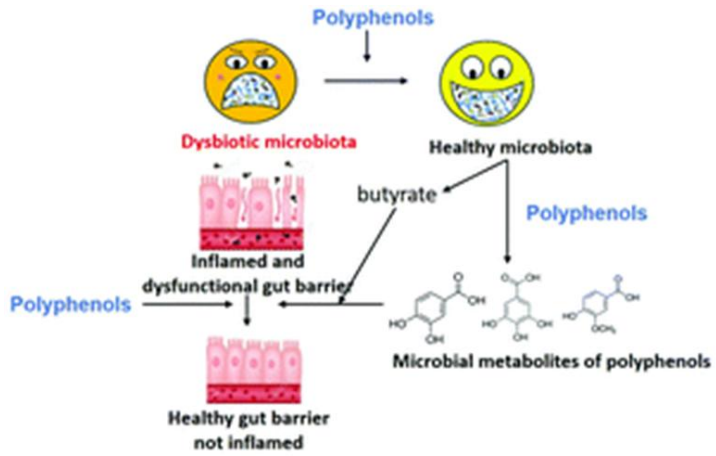




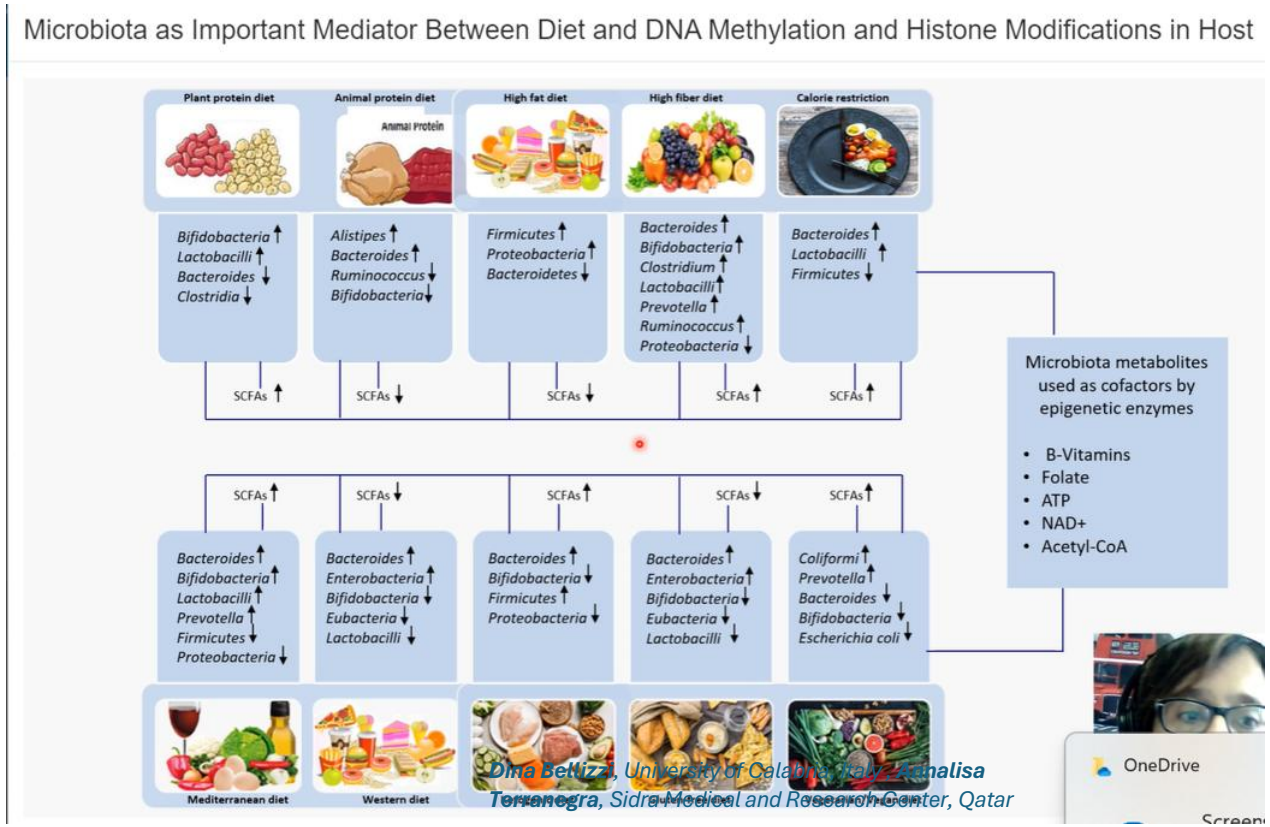
Eine hohe individuelle Diversität der Darm- Mikrobiota spiegelt Ernährung und Lebensstil wider und führt zu einer unterschiedlichen Produktion von Metaboliten, insbesondere von SCFAs



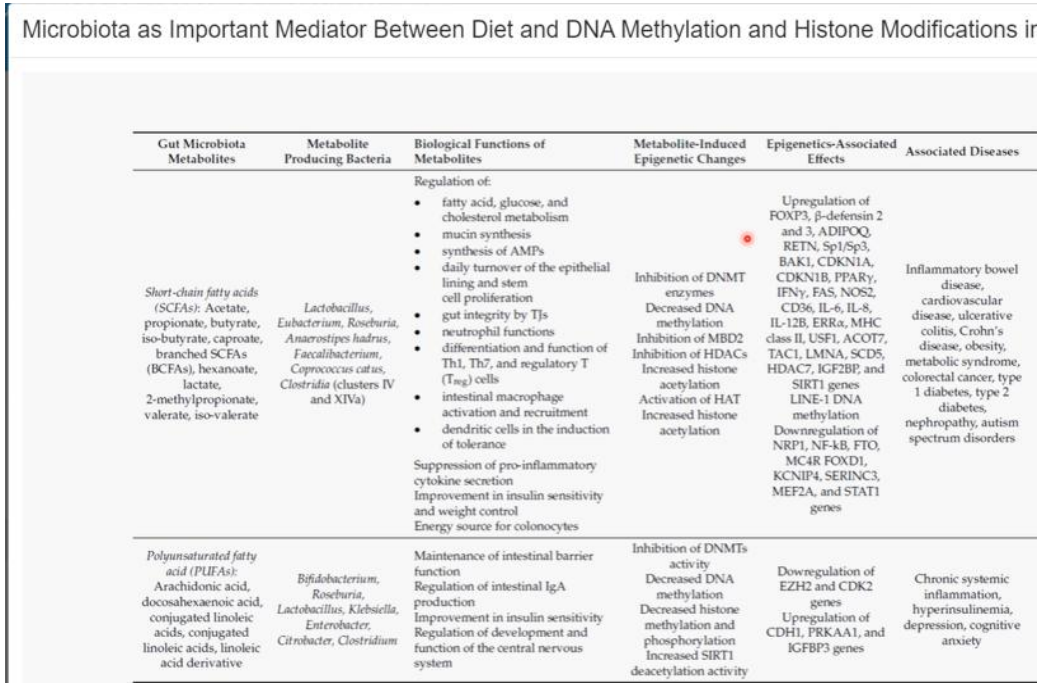




Mikrobiota und deren Metabolite sind wichtige Mediatoren zwischen Ernährung und epigenetischer Regulation. Welche Diät beeinflusst welche Bakterien, welche Metabolite und deren epigenetische Wirkung



Dina Bellizzi, University of Calabria, Italy; Annalisa Terranegra, Sidra Medical and Research Center, Qatar

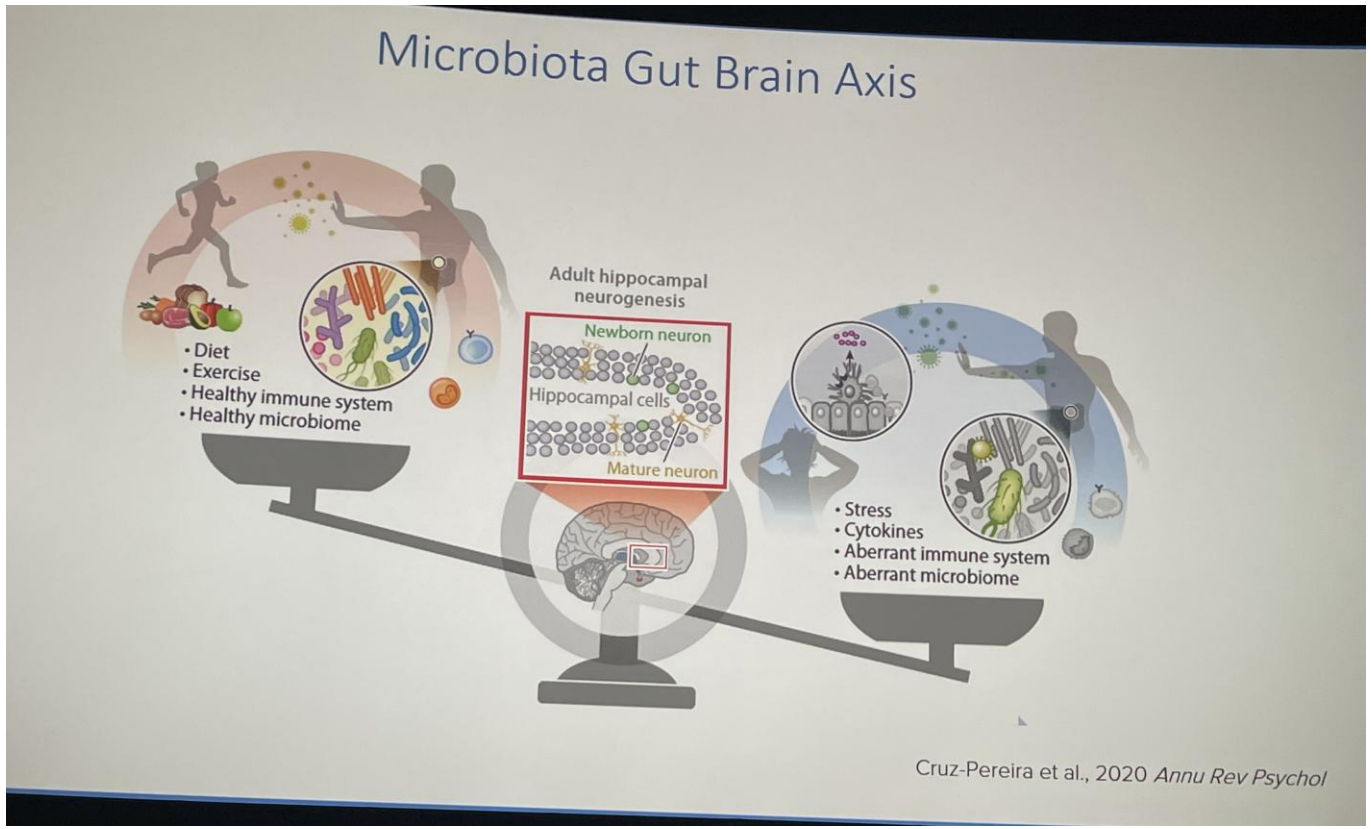

Microbiota as Important Mediator Between Diet and DNA Methylation and Histone Modifications ir

Gut Microbiota Metabolites	Metabolite Producing Bacteria	Biological Functions of Metabolites	Metabolite-Induced Epigenetic Changes	Epigenetics-Associated Effects	Associated Diseases
Short-chain fatty acids (SCFAs): Acetate, propionate, butyrate, iso-butyrate, caproate, branched SCFAs (BCFAs), hexanoate, lactate, 2-methylpropionate, valerate, iso-valerate	*Lactobacillus, Eubacterium, Roseburia, Anaerostipes hadrus, Faecalibacterium, Coprococcus catus, Clostridia* (clusters IV and XIVa)	Regulation of: • fatty acid, glucose, and cholesterol metabolism • mucin synthesis • synthesis of AMPs • daily turnover of the epithelial lining and stem cell proliferation • gut integrity by TJs • neutrophil functions • differentiation and function of Th1, Th7, and regulatory T (T_{reg}) cells • intestinal macrophage activation and recruitment • dendritic cells in the induction of tolerance Suppression of pro-inflammatory cytokine secretion Improvement in insulin sensitivity and weight control Energy source for colonocytes	Inhibition of DNMT enzymes Decreased DNA methylation Inhibition of MBD2 Inhibition of HDACs Increased histone acetylation Activation of HAT Increased histone acetylation	Upregulation of FOXP3, β-defensin 2 and 3, ADIPOQ, RETN, Sp1/Sp3, BAK1, CDKN1A, CDKN1B, PPARγ, IFNγ, FAS, NOS2, CD36, IL-6, IL-8, IL-12B, ERRα, MHC class II, USF1, ACOT7, TAC1, LMNA, SCD5, HDAC7, IGF2BP, and SIRT1 genes LINE-1 DNA methylation Downregulation of NRP1, NF-kB, FTO, MC4R FOXD1, KCNIP4, SERINC3, MEF2A, and STAT1 genes	Inflammatory bowel disease, cardiovascular disease, ulcerative colitis, Crohn's disease, obesity, metabolic syndrome, colorectal cancer, type 1 diabetes, type 2 diabetes, nephropathy, autism spectrum disorders
Polyunsaturated fatty acid (PUFAs): Arachidonic acid, docosahexaenoic acid, conjugated linoleic acids, conjugated linoleic acids, linoleic acid derivative	*Bifidobacterium, Roseburia, Lactobacillus, Klebsiella, Enterobacter, Citrobacter, Clostridium*	Maintenance of intestinal barrier function Regulation of intestinal IgA production Improvement in insulin sensitivity Regulation of development and function of the central nervous system	Inhibition of DNMTs activity Decreased DNA methylation Decreased histone methylation and phosphorylation Increased SIRT1 deacetylation activity	Downregulation of EZH2 and CDK2 genes Upregulation of CDH1, PRKAA1, and IGFBP3 genes	Chronic systemic inflammation, hyperinsulinemia, depression, cognitive anxiety

SESSION 3: Mental HEALTH

Lifestyle factors and the gut-brain axis: relevance to Alzheimer's Neurogenese

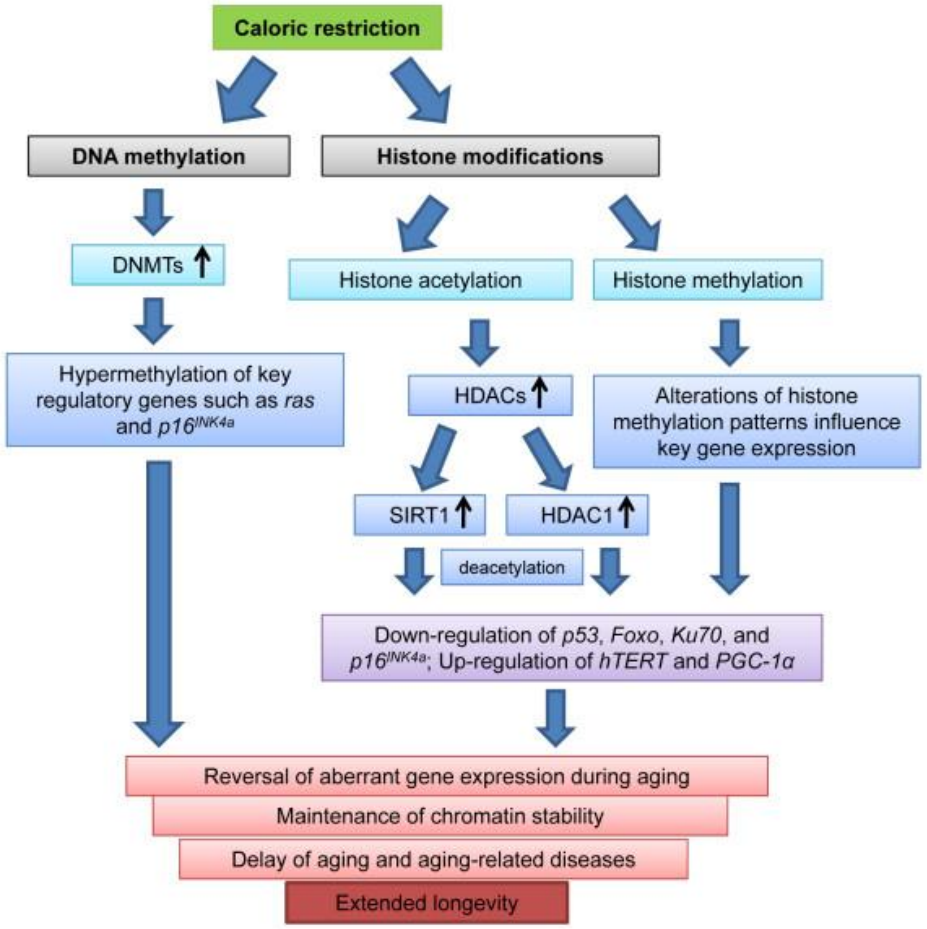
Prof. Yvonne Nolan, University Cork, Ireland

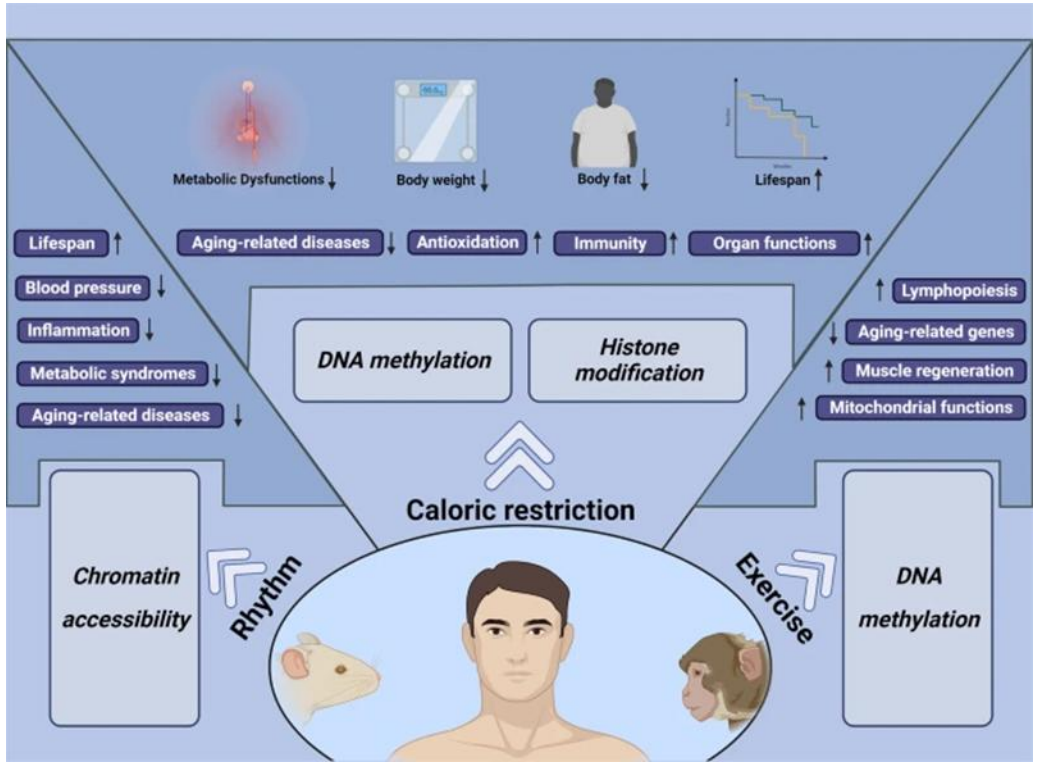


Mikrobiota mit Einfluss auf die Neurogenese im Hippokampus

Yakult Science for Health

Beste Diät: Fasten > 3 d, Epigenetik: HDACs, Sirts, mTor, Butyrat, BHB





Fasten- Mimetika, Mikrobiota und Epigenetik, Study design

STOFF	WIRKSTOFF	MENGE / 25ML	Wirkstoff
Blueberry Extract	Anthocyanins/ Anthocyanidin..	40 mg	14mg 10mg
Broccoli Extract	Sulpharapane, Glucoraphin..	30 mg	
Apfel extract	Phlorentin, Quercetin..	50 mg	
Citrus extract	Naringin..	40 mg	
Nikotinamid	Nikotinamid ribosid	24 mg	
Zinkgluconat	Zink	7.5 mg	

Wasser, Stevia, Erythrit

Buchinger Fasting < 250 kcal/day
n: 22 in Pernegg Monastery

Feces , blood spots, before and After the end, first solid feces

Active (N. 131) Placebo (n: 30)
Intervention 3 months

Feces, Blood spots before, after 1,3 month

Illuminia sequencing, Line 1 methylation bisulfite
qPCR, HR-MCA, RNA, MiRNA RT QPCRi

Conclusions

In conclusion fasting and to some extend fasting mimetics result in beneficial modulation of microbiota (e.g diversity, SCFA, BHP) and metabolism (e.g SIRTS, mtDNA, telomer length)

Microbiota structure seems to interfere with the expression of Sirtuins and metabolism relevant miRNAs

Hindawi
Oxidative Medicine and Cellular Longevity
Volume 2020, Article ID 4793125, 13 pages
https://doi.org/10.1155/2020/4793125

Hindawi

Research Article

Epigallocatechin Gallate Effectively Affects Senescence and Anti-SASP via *SIRT3* in 3T3-L1 Preadipocytes in Comparison with Other Bioactive Substances

Stephanie Lilja,[1] Julia Oldenburg,[1] Angelika Pointner,[1] Laura Dewald,[1] Mariam Lerch,[1] Berit Hippe,[2] Olivier Switzeny,[2] and Alexander Haslberger[1]

International Journal of *Molecular Sciences*

MDPI

Article

Five Days Periodic Fasting Elevates Levels of Longevity Related *Christensenella* and Sirtuin Expression in Humans

Online ISSN: 2160-3855, Print ISSN: 2378-7007
Functional Foods in Health and Disease
Home Editorial Team Iss

Duszka [1], Tewodros Debebe [2],
slberger [1,*]

Home > Vol 10, No 10 (2020) > Lilja

Fasting and fasting mimetic supplementation address sirtuin expression, miRNA and microbiota composition

Stephanie Lilja, Hanna Bäck, Kalina Duszka, Berit Hippe, Lucia Suarez, Ingrid Höfinger, Tewodros Debebe, Jürgen König, Alexander Haslberger

Bioactive Compounds in Health and Disease 2021; 4(4): 45-62 BCHD Page 45 of 62

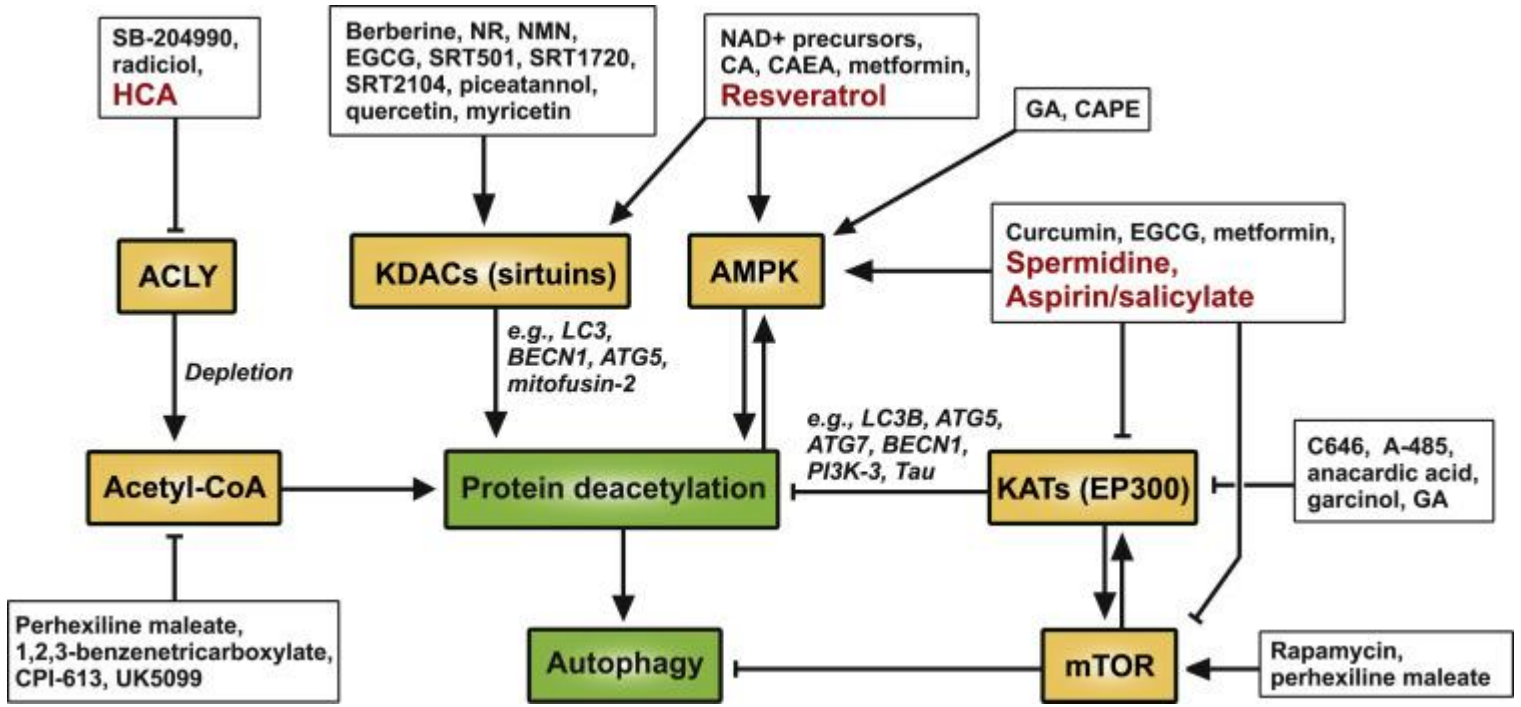
Research Article Open Access

BCHD
Bioactive Compounds in Health and Disease

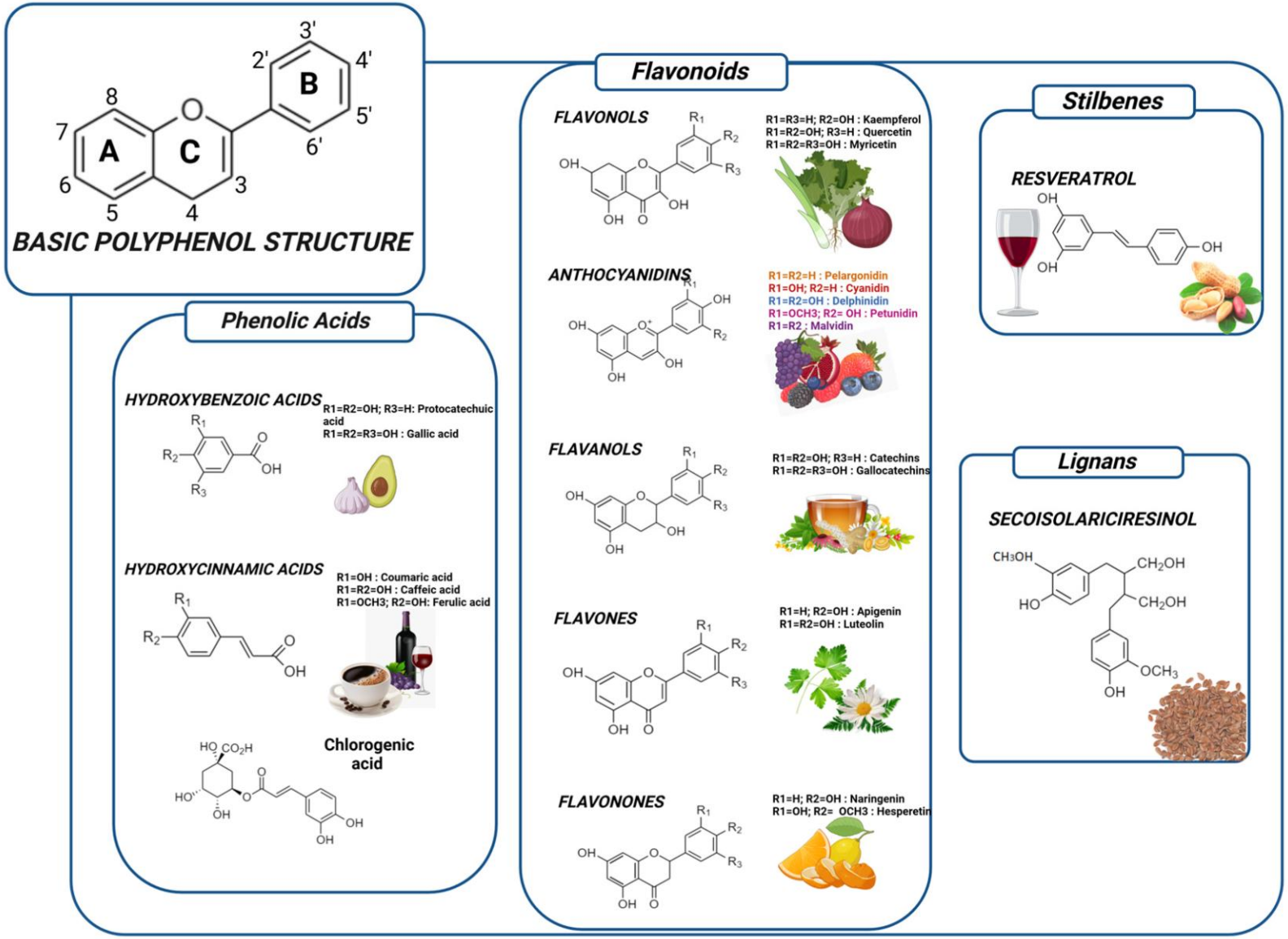
Increased Sirtuin expression, senescence regulating miRNAs, mtDNA, and bifidobacteria correlate with wellbeing and skin appearance after Sirtuin- activating drink

Stephanie Lilja, Hanna Bäck, Carinna Stoll, Anna Mayer, Angelika Pointner, Berit Hippe, Ulrike Krammer, Alexander G. Haslberger*

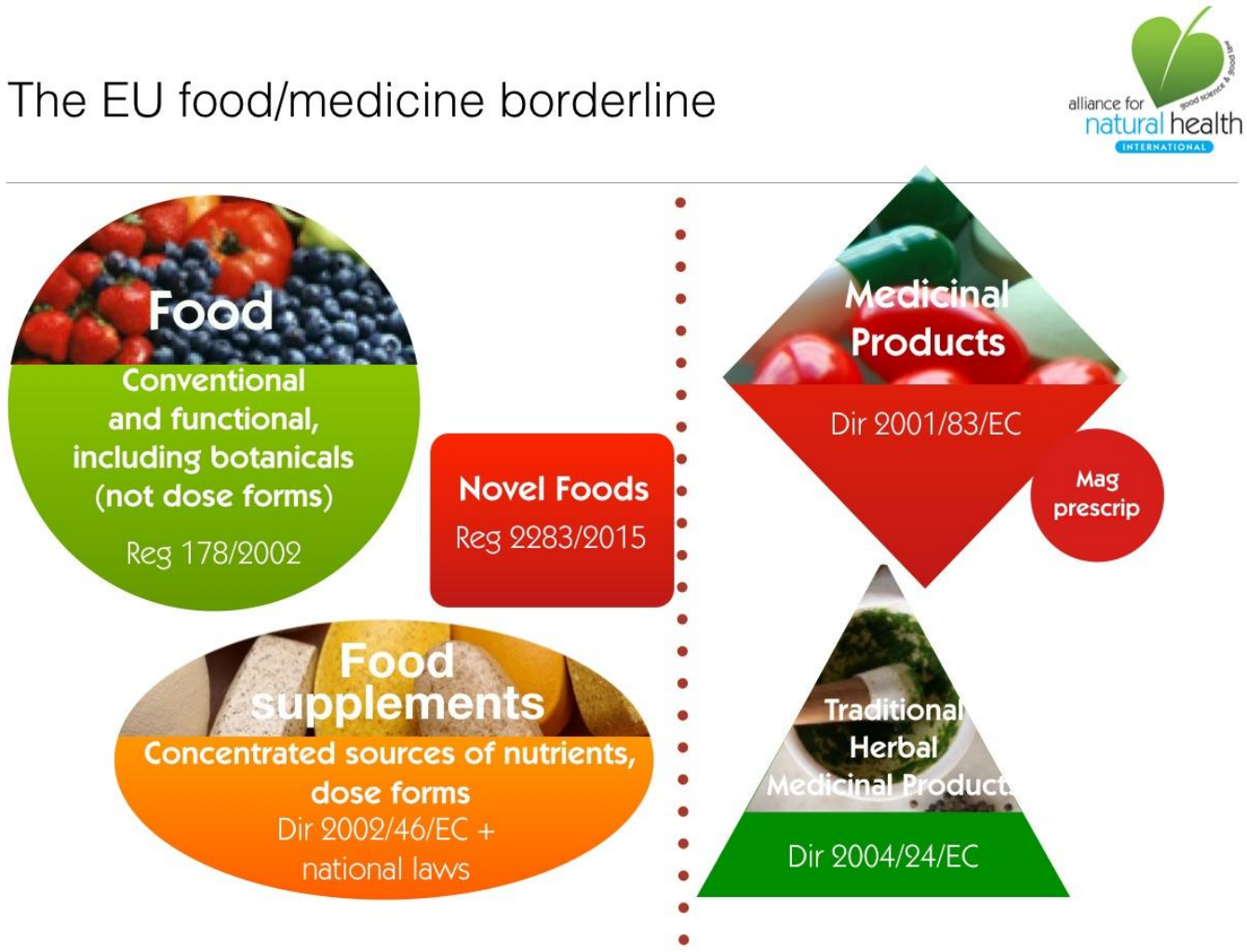
Fasting- Mimetika und Epigenetik, Nutrazeutika and Pharmazeutika



Polyphenole und ihre pflanzlichen Quellen

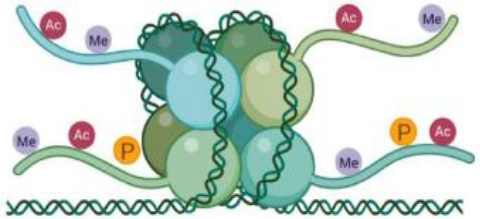


Viele Namen und Gesetze



Polyphenole adressieren alle Elemente des epigenetischen Systems

DNA Methylation | Histone Modifications | miRNA



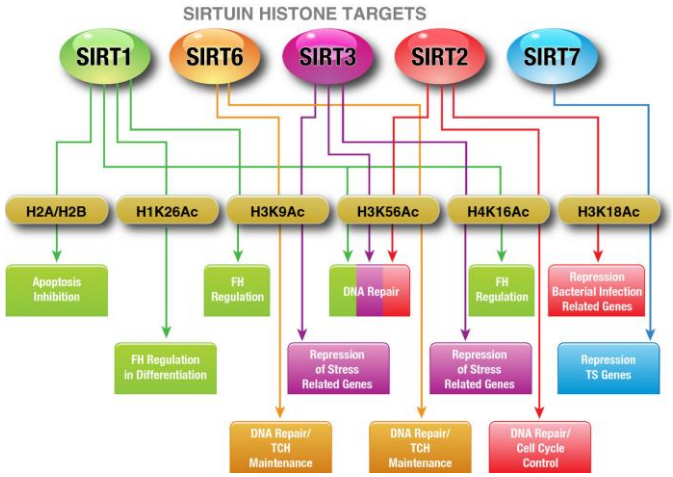
DNA Methyl Transferase
Capsaicin
Curcumin
Diallyl Sulphide
Luteolin

Histone Acetylation
6-Shogoal
Anethole
Capsaicin
Curcumin
Diallyl disulphide
Diallyl trisulphide
Garcinol
Lapiferin
Luteolin
Sesamin
α Mangostin
γ Bisabolene

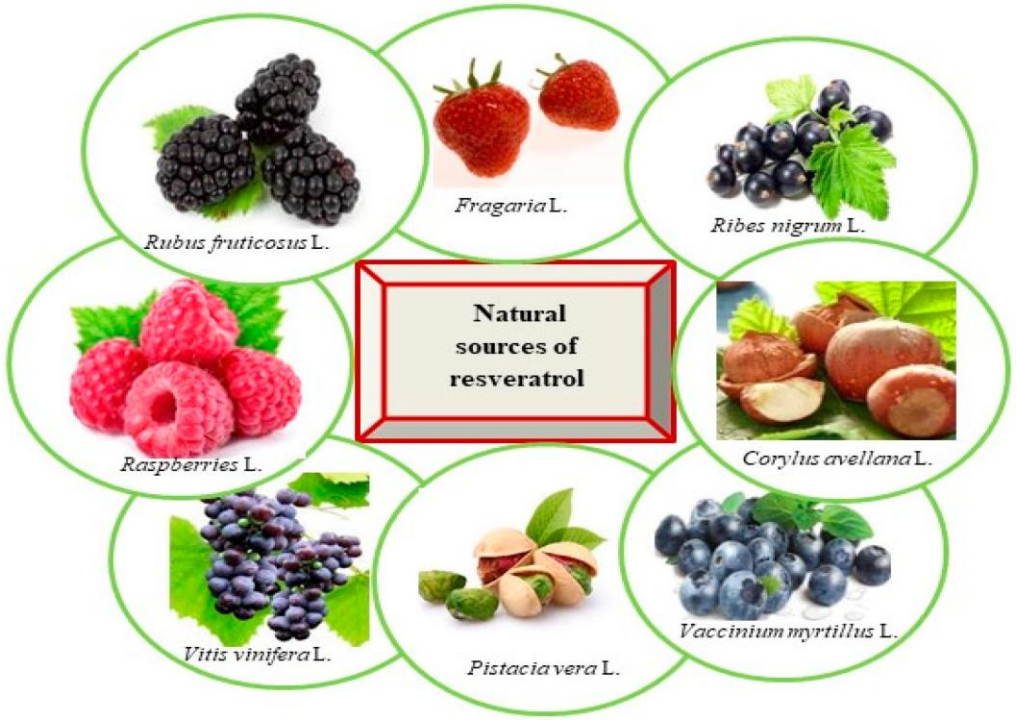
Histone Methylation
Basil Polysaccharides
Luteolin

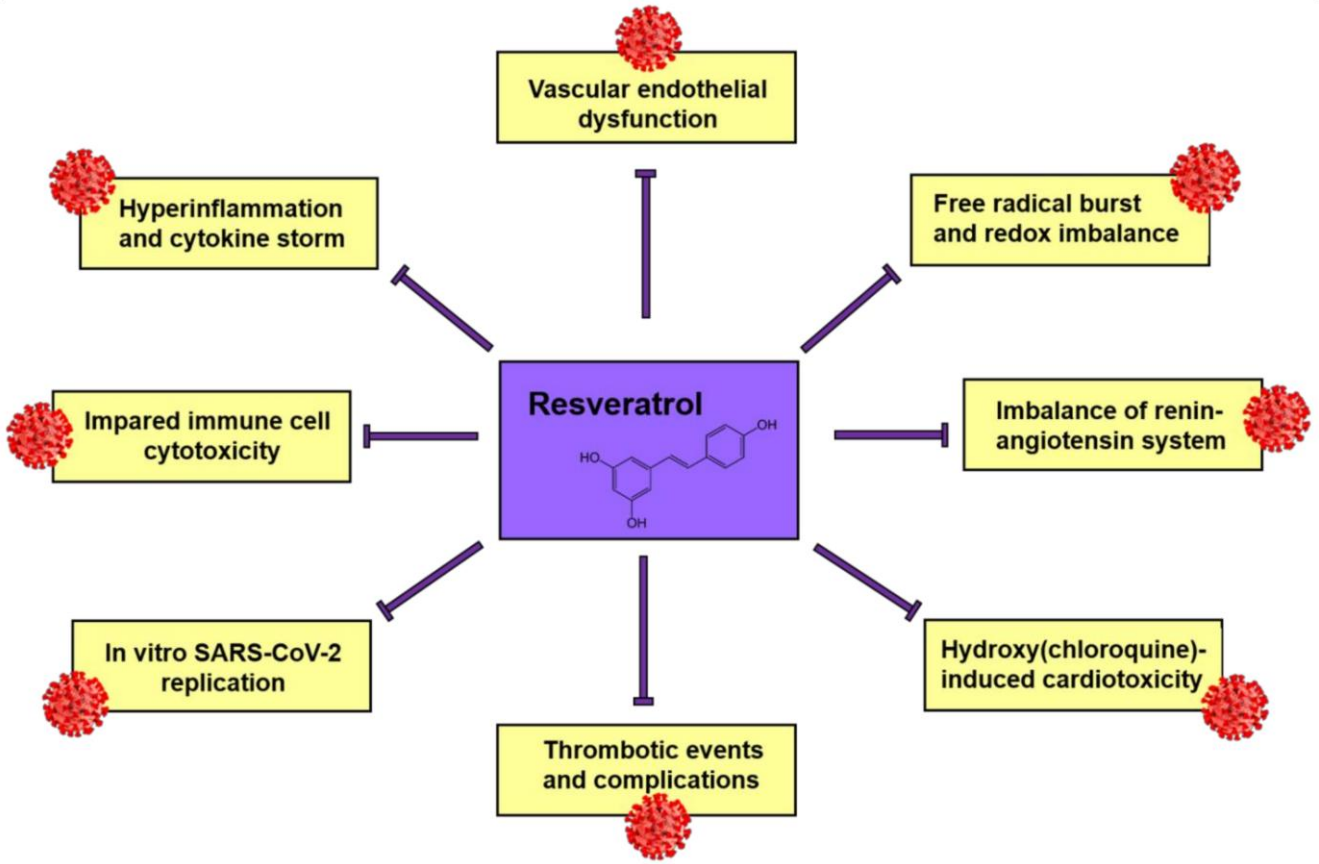
Histone Phosphorylation
Luteolin

mi RNA Expression
1-Acetoxy chavicol
Apigenin
Capsaicin
Curcumin
Diallyl trisulphide
Garcinol
Luteolin
α Mangostin



Resveratrol





EGCG

Epigallocatechin gallate (EGCG) is a unique plant compound that may help to reduce inflammation, aid weight loss, and prevent conditions like heart disease. Epigallocatechin gallate (EGCG) is a type of plant-based compound called catechins, which are a type of polyphenol.

Research Article

EGCG Prevents High Fat Diet-Induced Changes in Gut Microbiota, Decreases of DNA Strand Breaks, and Changes in Expression and DNA Methylation of *Dnmt1* and *MLH1* in C57BL/6J Male Mice

Marlene Remely,[1] Franziska Ferk,[2] Sonja Sterneder,[1] Tahereh Setayesh,[2] Sylvia Roth,[1] Tatjana Kepcija,[1] Rahil Noorizadeh,[2] Irene Rebhan,[1] Martina Greunz,[1] Johanna Beckmann,[1] Karl-Heinz Wagner,[1] Siegfried Knasmüller,[2] and Alexander G. Haslberger[1]

Research Article

Epigallocatechin Gallate Effectively Affects Senescence and Anti-SASP via *SIRT3* in 3T3-L1 Preadipocytes in Comparison with Other Bioactive Substances

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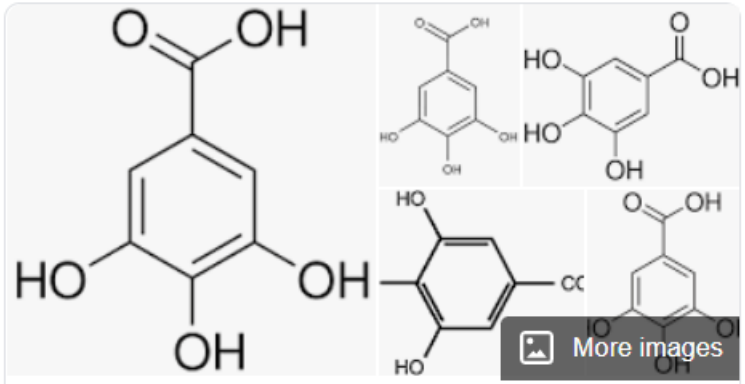
Gallic acid

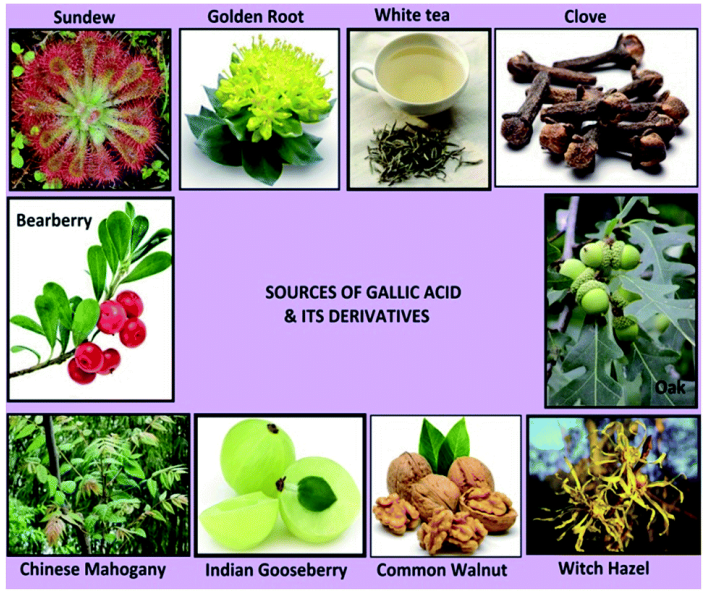


Gallic acid

Gallic acid is a trihydroxybenzoic acid with the formula $C_6H_2(OH)_3CO_2H$. It is classified as a phenolic acid. It is found in gallnuts, sumac, witch hazel, tea leaves, oak bark, and other plants. It is a white solid, although samples are typically brown owing to partial oxidation.
Wikipedia

Gallic acid, a common dietary phenolic protects against high fat diet induced DNA damage

Tahereh Setayesh[1] · Armen Nersesyan[1] · Miroslav Mišík[1] · Rahil Noorizadeh[1,3] · Elisabeth Haslinger[1] · Tahereh Javaheri[2,3] · Elisabeth Lang[1] · Michael Grusch[1] · Wolfgang Huber[1] · Alexander Haslberger[4] · Siegfried Knasmüller[1]



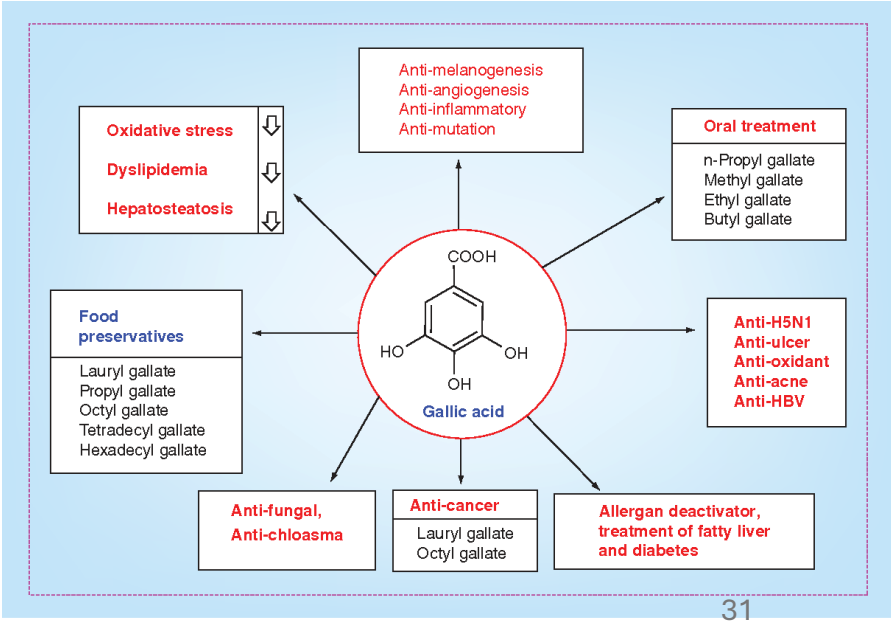


Figure 2. Important uses of gallic acid and its ester derivatives.

Astaxanthin

Astaxanthin

Chemical compound

Astaxanthin is a keto-carotenoid with various uses including dietary supplement and food dye. It belongs to a larger class of chemical compounds known as terpenes built from five carbon precursors, isopentenyl diphosphate, and dimethylallyl diphosphate. Wikipedia

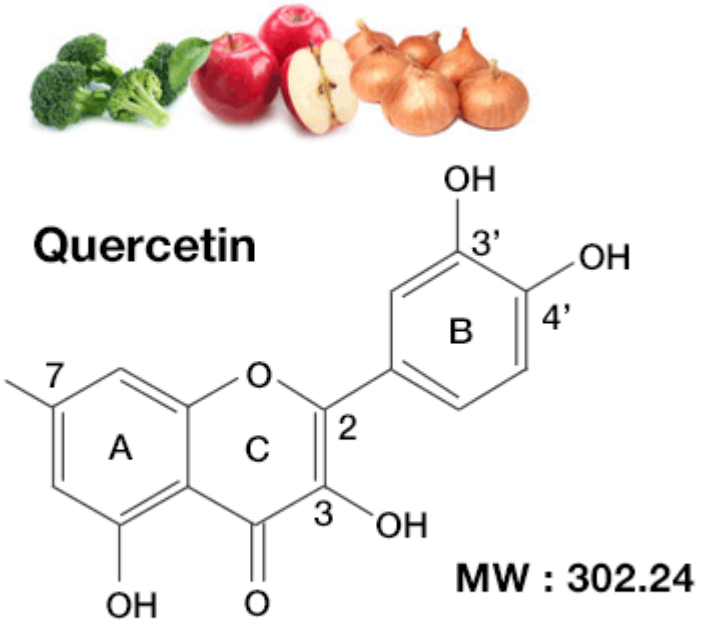
Astaxanthin ist ein natürlicher, orangeroter Farbstoff. Er zählt zu den Carotinoiden, genauer gesagt zu den sauerstoffhaltigen Xanthophyllen. Das sind farbige Inhaltsstoffe bestimmter Pflanzen. Es wurde früher auch als Hämatochrom bezeichnet (von altgriechisch „haima“ für „Blut“ und „chroma“ für „Farbe“). Die Substanz wird hauptsächlich von Mikroalgen wie der Blutregenalge (Haematococcus pluvialis), aber auch der roten Hefe Phaffia rhodozyma und dem Bakterium Paracoccus carotinifaciens gebildet.1

Astaxanthin dient der Alge als natürlicher UV-Schutz und als Molekül zur Nährstoffbindung: Um unter schwierigen Umweltbedingungen wie starker Sonneneinstrahlung, Wasser- oder Sauerstoffmangel zu überleben, stellt sie ihre Stoffwechselvorgänge ein und bildet zum Schutz eine blutrote Zyste, deren Pigmente aus Astaxanthin bestehen.2

Das Carotinoid ist jedoch nicht nur im Plankton enthalten, sondern gelangt über die Nahrungskette in das Tierreich. Wassertiere wie Lachs, Garnelen, Forellen, Krill oder Krebse, aber auch Flamingos fressen die Mikroalge. Sie erhalten durch Astaxanthin ihre rötliche Färbung und schützen sich damit ebenfalls vor den schädlichen Auswirkungen von UV-Licht und aggressiven Sauerstoffradikalen.3 Der Nährstoff ist auch ein wichtiger Zusatz in Futtermitteln und hilft bei der gesunden Aufzucht von Jungfischen.4

Quercetin, plant flavonol

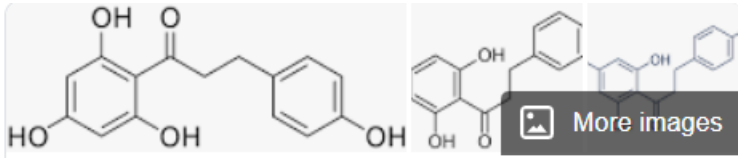
[Various physiological functions of quercetin]



Antioxidant effect | Lipid reduction effect
Anti-inflammation effect | Hypotensive effect
Anti-cancer effect | Anti-obesity effect

Quercetin Benefits	Additional Information
Anti-inflammatory and Immune Boosting Research has shown that quercetin displays anti-inflammatory and immune strengthening capabilities. One study even shows how quercetin was able to mitigate the inflammatory responses stimulated by the popular food additive carrageenan. Quercetin was also shown to be able to decrease the clinical indicators of arthritis.	**Recommended daily intake** • 200-250 mg/day or even lower. • Research shows that even small amounts are effective for everyday consumption.
Possible Cancer fighting properties Studies have shown that quercetin was able to restrain the growth of cancer and as such prevent the proliferation of cancer cells especially as it relates to certain types of cancers – colorectal, ovarian and breast cancer cells.	**Some foods that are high in quercetin** • Onions • Shallots • Asparagus • Green peppers • Tomatoes • Apples • Cranberries
Cardiovascular Health Research shows that quercetin was able to reduce some of the major risks factors of heart disease such as high blood pressure, oxidative stress and inflammation.	
Anti-viral properties Studies have shown that quercetin was effective in the prevention of viral or respiratory conditions as well as well as fight against viruses such as herpes and parainfluenza type 3. **Asthma** Research shows that quercetin is able to reduce inflammatory cells of the immune system as well as decrease the histamine levels which then helps to smooth the muscles of the airways and helps with breathing.	**Possible side effects** • Headaches • Stomach discomfort • Kidney damage (high doses). 
Almondsandolivez.com	

Phloretin



Phloretin

Phloretin is a dihydrochalcone, a type of natural phenol. It can be found in apple tree leaves and the Manchurian apricot. Wikipedia

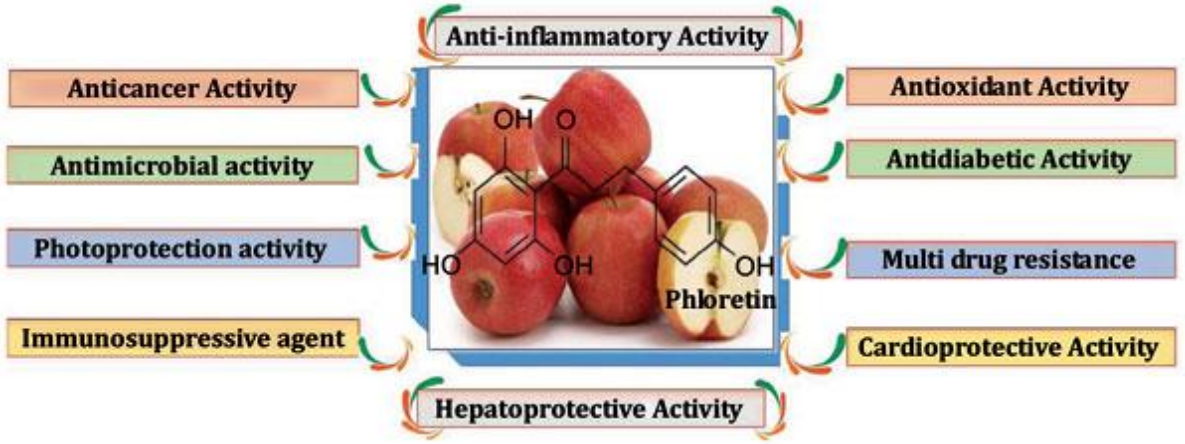


Tabelle 1. Potenzielle chemopräventive Aktivitäten der Apfelsaftextrakte A und B[a]

	Extrakt A	Extrakt B
Mechanismen in der Initiationsphase		
DPPH-Radikalfängereigenschaften (IC_{50})[b]	8.7 µg/ml	10.5 µg/ml
Peroxyl-Radikalfängereigenschaften (ORACROO)(Einheiten)[d]	2.4	1.9
Superoxid Anion Radikalfängereigenschaften (IC_{50})	17.1 µg/ml	25.8 µg/ml
Hemmung der Cyp1A Aktivität (IC_{50})[b]	11.5 µg/ml	4.3 µg/ml
Induktion der NAD(P)H:Chinon-Reduktase-Aktivität in Hepa1c1c7-Maus-Hepatomzellen (CD)[c]	200 µg/ml	39.2 µg/ml
Hemmung der Hepa1c1c7-Zellproliferation (IC_{50})	>200 µg/ml	>200 µg/ml
Anti-Tumorpromovierende Mechanismen		
Hemmung der Aromatase Aktivität (IC_{50})	5.9 µg/ml	5.0 µg/ml
Hemmung der Cox-1-Aktivität (% Hemmung bei 400 µg/ml)	62	74
Anti-proliferative Mechanismen		
Hemmung der Proliferation von humanen HCT116-Darmkrebszellen (IC_{50})	44.3 µg/ml	35.3 µg/ml

[a] Beschreibung der Testsysteme in Gerhauser et al. 2003

Phloretin II, interindividuelle Variationen in der Phloretin Absorption und im Stoffwechsel

Food & Function

ROYAL SOCIETY OF CHEMISTRY

PAPER

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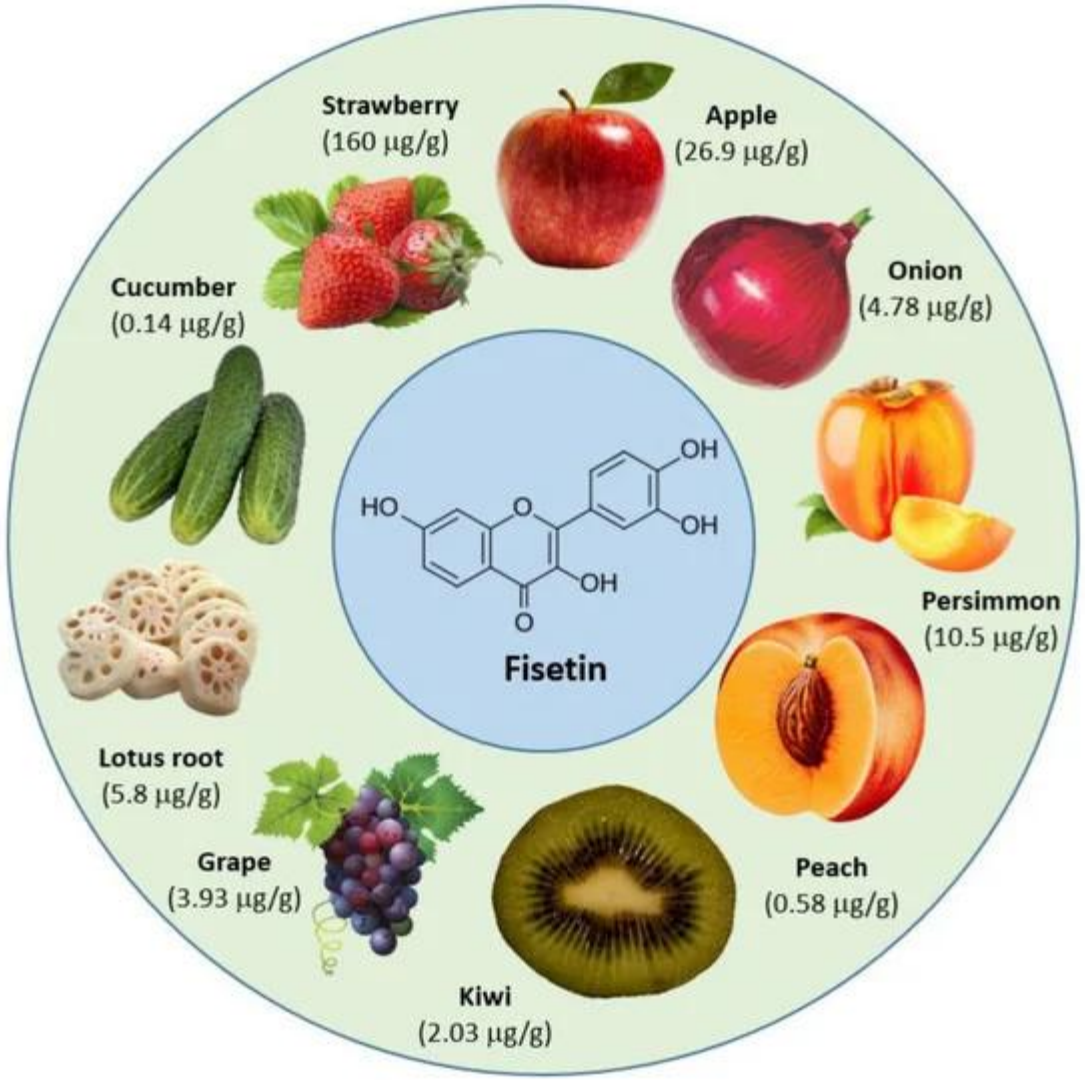
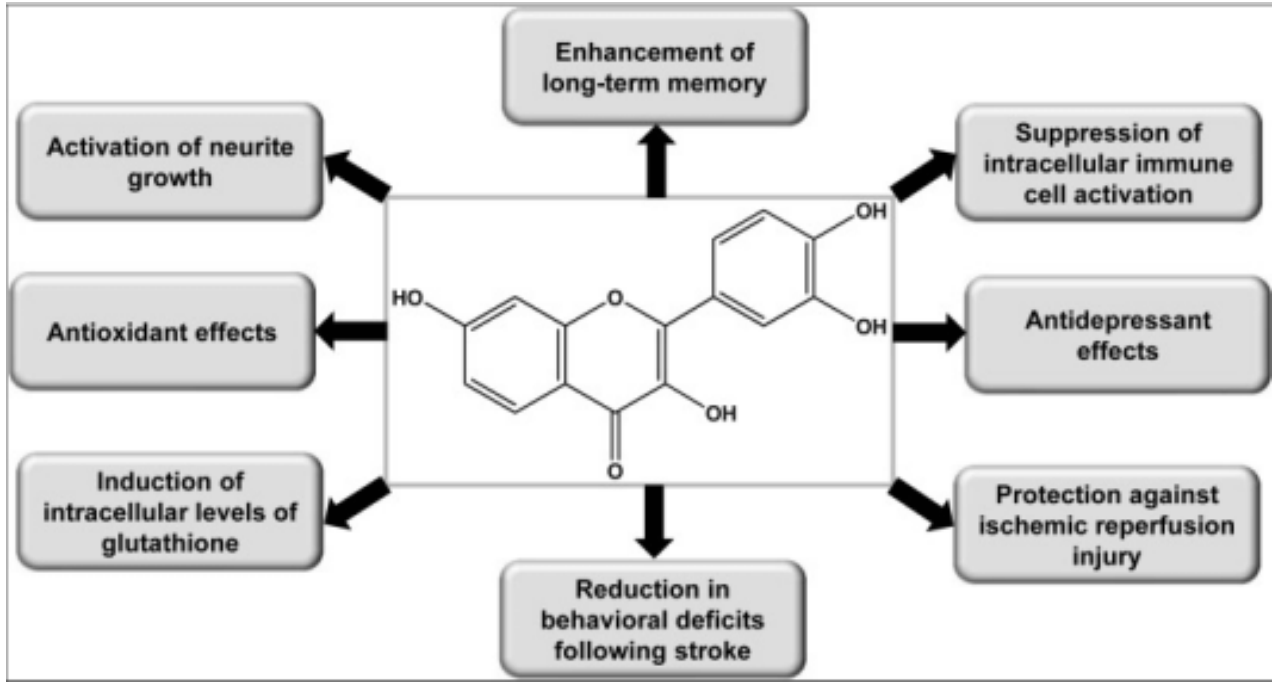
Cite this: DOI: 10.1039/d3fo02985a

Assessment of human inter-individual variability of phloretin metabolites in urine after apple consumption. AppleCOR study†

extensive interindividual variability exists in the excretion of phloretin phase-II conjugates following consumption of apple snacks, which could be related to oral microbiota phloridzin-hydrolysing activity, lactase non-persistence trait or the metabotype to which the subject belongs. There were inconsistent effects on postprandial serum glucose concentrations but there was a tendency for decreases to be associated with higher excretion of phloretin phase-II conjugates.

Fisetin


Strawberry
(160 μg/g)
Apple
(26.9 μg/g)
Onion
(4.78 μg/g)
Cucumber
(0.14 μg/g)
Persimmon
(10.5 μg/g)
Lotus root
(5.8 μg/g)
Grape
(3.93 μg/g)
Peach
(0.58 μg/g)
Kiwi
(2.03 μg/g)
Fisetin

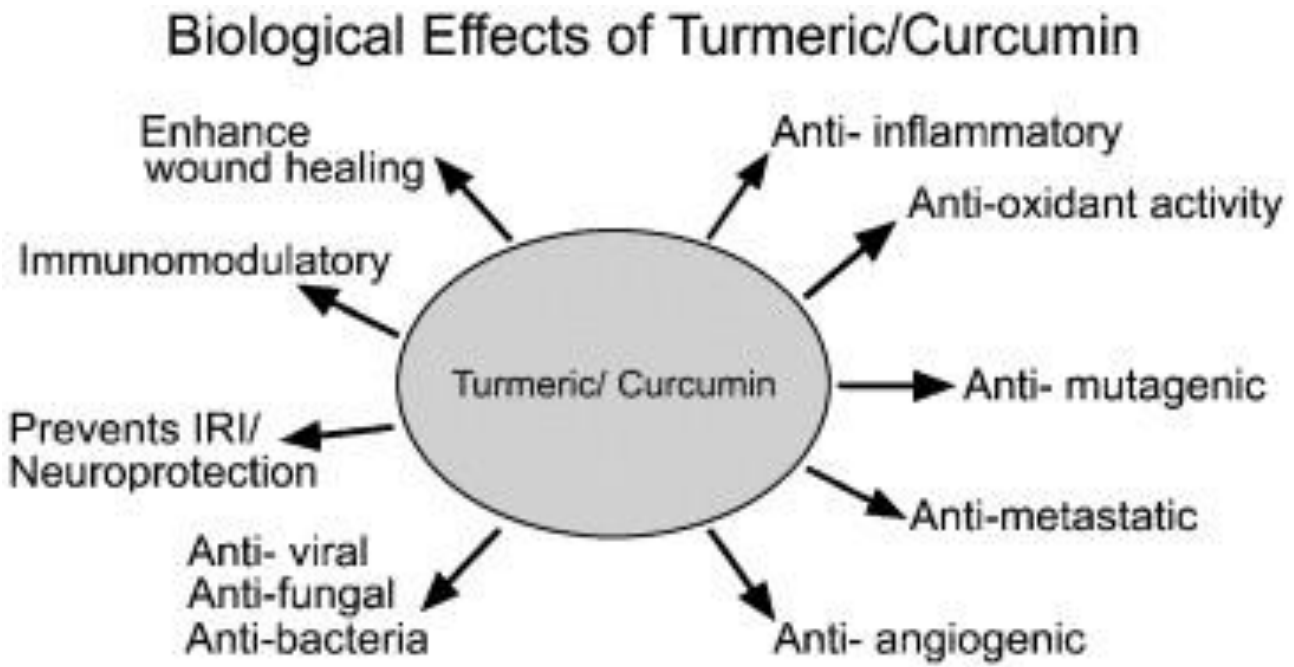

Enhancement of long-term memory
Activation of neurite growth
Suppression of intracellular immune cell activation
Antioxidant effects
Antidepressant effects
Induction of intracellular levels of glutathione
Protection against ischemic reperfusion injury
Reduction in behavioral deficits following stroke

Curcumin

Curcumin

Chemical compound

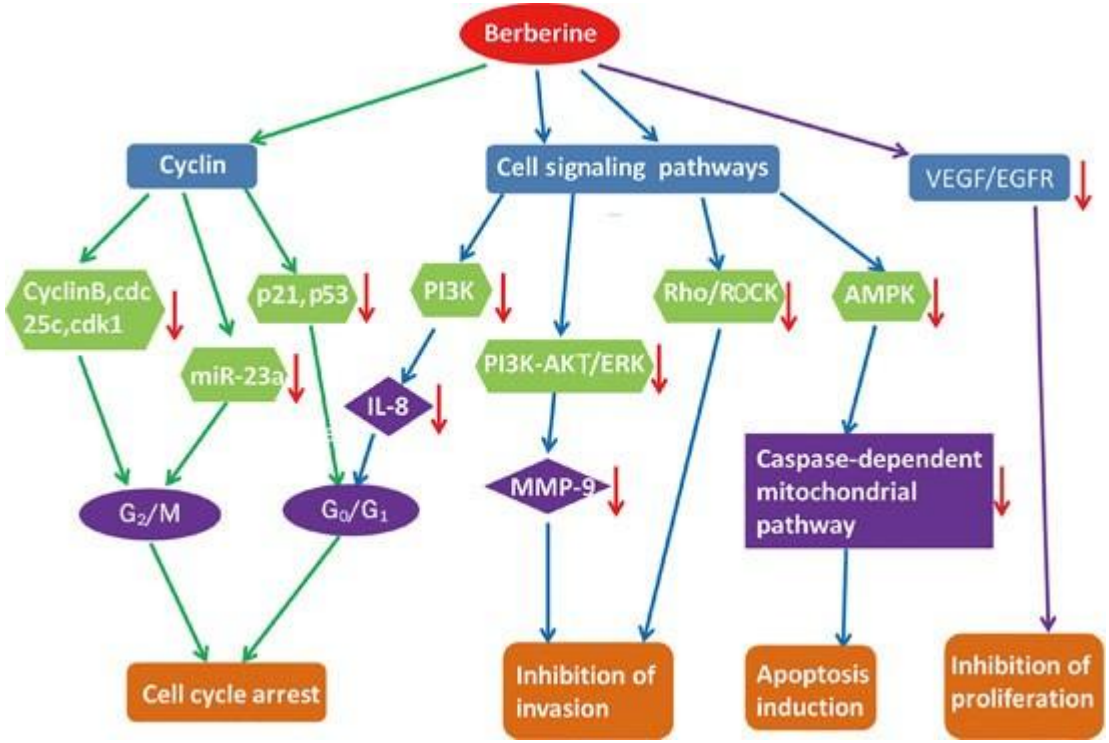
Curcumin is a bright yellow chemical produced by plants of the Curcuma longa species. It is the principal curcuminoid of turmeric, a member of the ginger family, Zingiberaceae. It is sold as an herbal supplement, cosmetics ingredient, food flavoring, and food coloring. Wikipedia



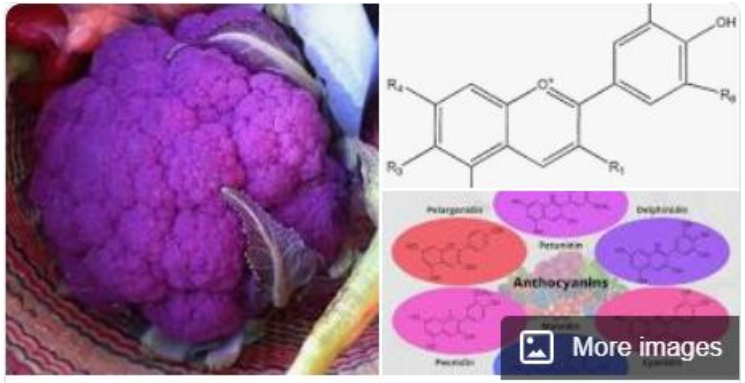
Berberin, Berberitze

Berberine (Berberin)

Berberine is a quaternary ammonium salt from the protoberberine group of benzylisoquinoline alkaloids found in such plants as Berberis, such as Berberis vulgaris, Berberis aristata, Mahonia aquifolium, ...
Wikipedia



Anthocyans



Anthocyanin

Chemical compound

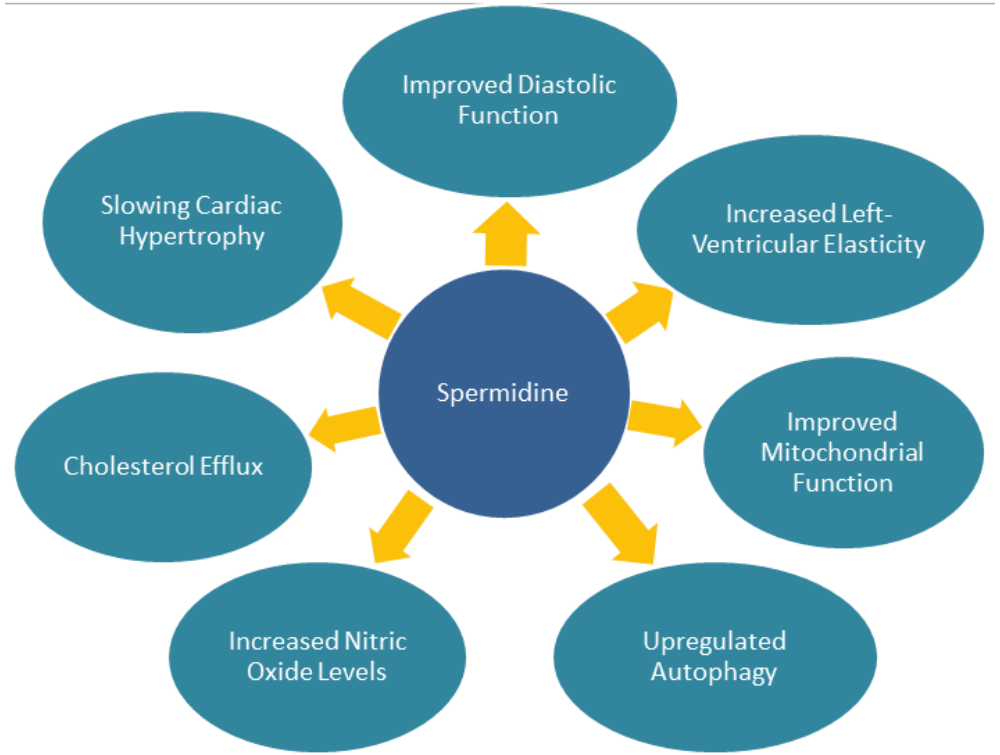
Anthocyanins are water-soluble vacuolar pigments that, depending on their pH, may appear red, purple, blue, or black. In 1835, the German pharmacist Ludwig Clamor Marquart gave the name Anthokyan to a chemical compound that gives flowers a blue color for the first time in his treatise “Die Farben der Blüthen”. Wikipedia

Spermidin (Polyamin)

Spermidine (Spermidin)

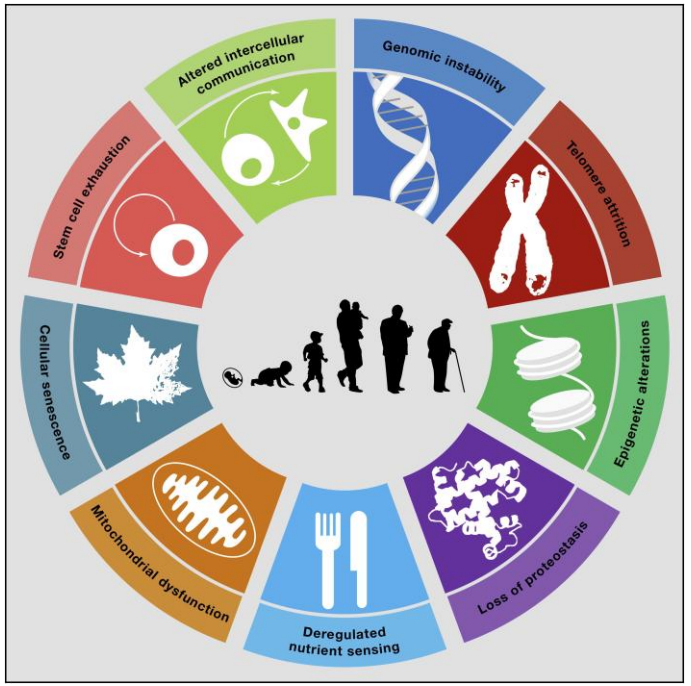
Chemical compound

Spermidine is a polyamine compound found in ribosomes and living tissues and having various metabolic functions within organisms. It was originally isolated from semen. Wikipedia

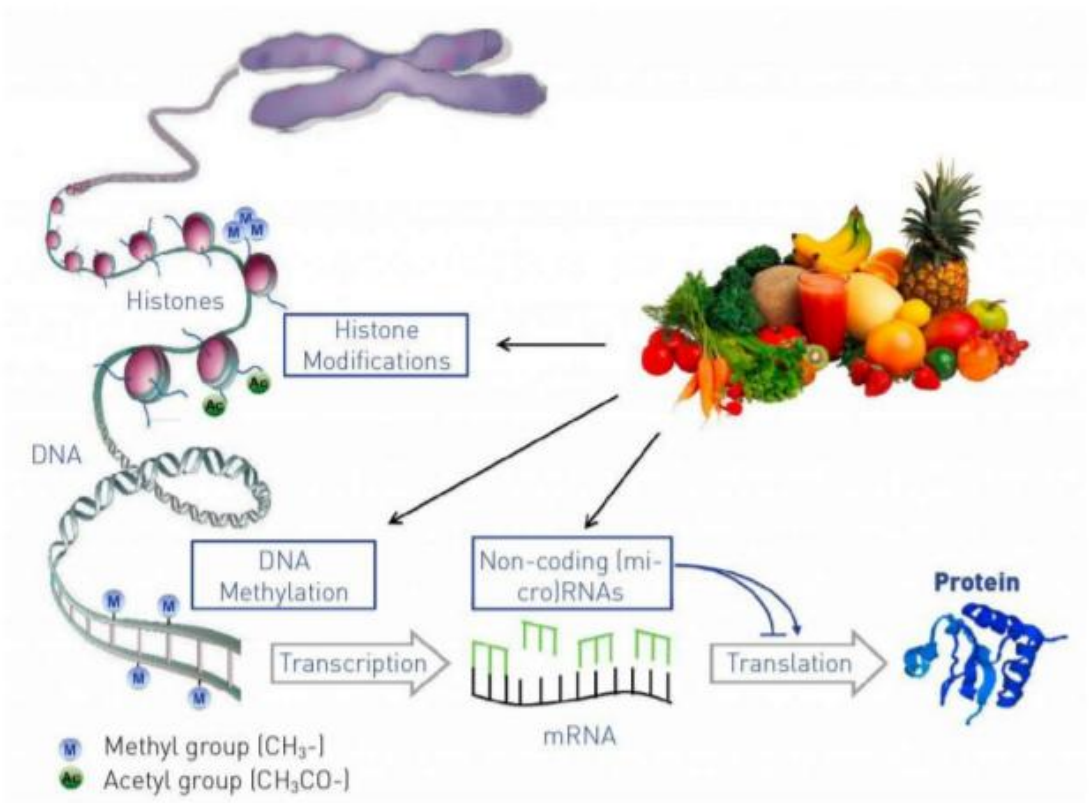


Diskutierte Aktivitäten von Nutrazeutika anhand der Hallmarks of aging , Fakten, Hypothesen ?

Anti oxydative	Epigenetic active
inflammation	neuroinflammation
Telomers	Mitochondria
Autophagy	Apoptose
Senolytic	DNa repair
Immune senescence	Nuro infl
Anti bacterial	Anti viral
AGING	



Pflanzeninhaltsstoffe regulieren alle Mechanismen und Epigenetik



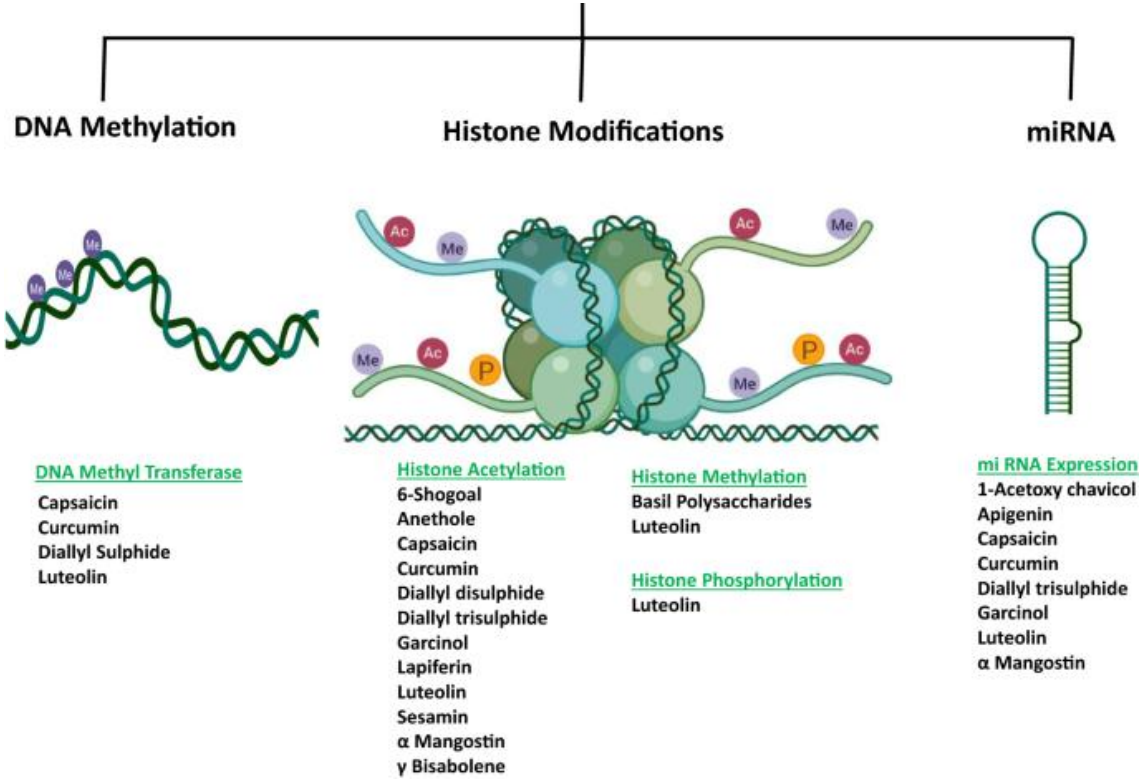
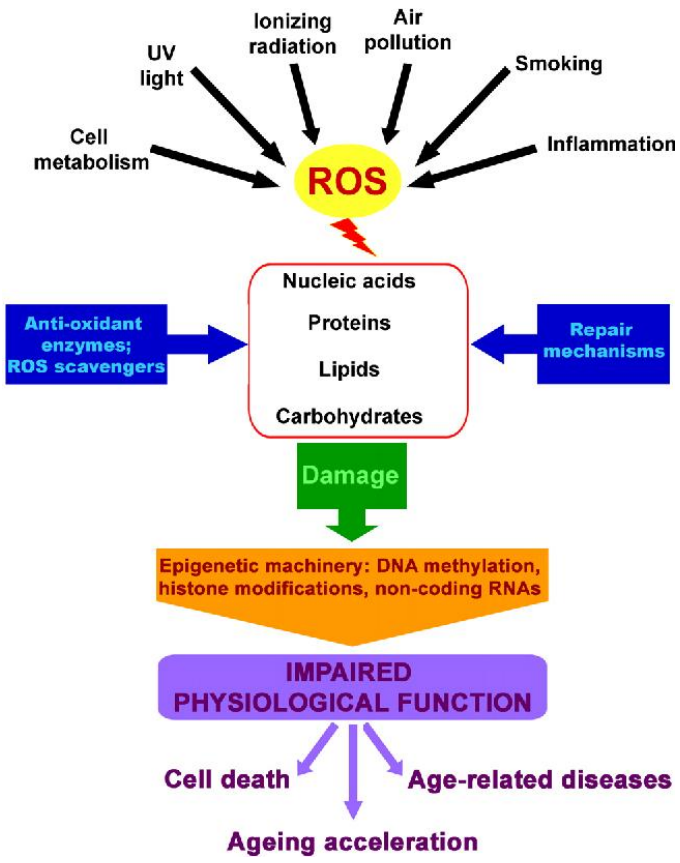
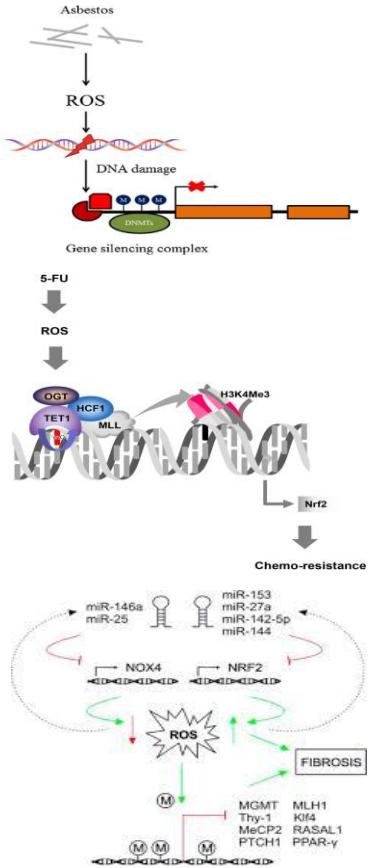


Figure 4. Polyphenols address all epigenetic mechanisms.

Ros, Stress beeinträchtigt alle Mechanismen der epigenetischen Maschinerie -> Alterung





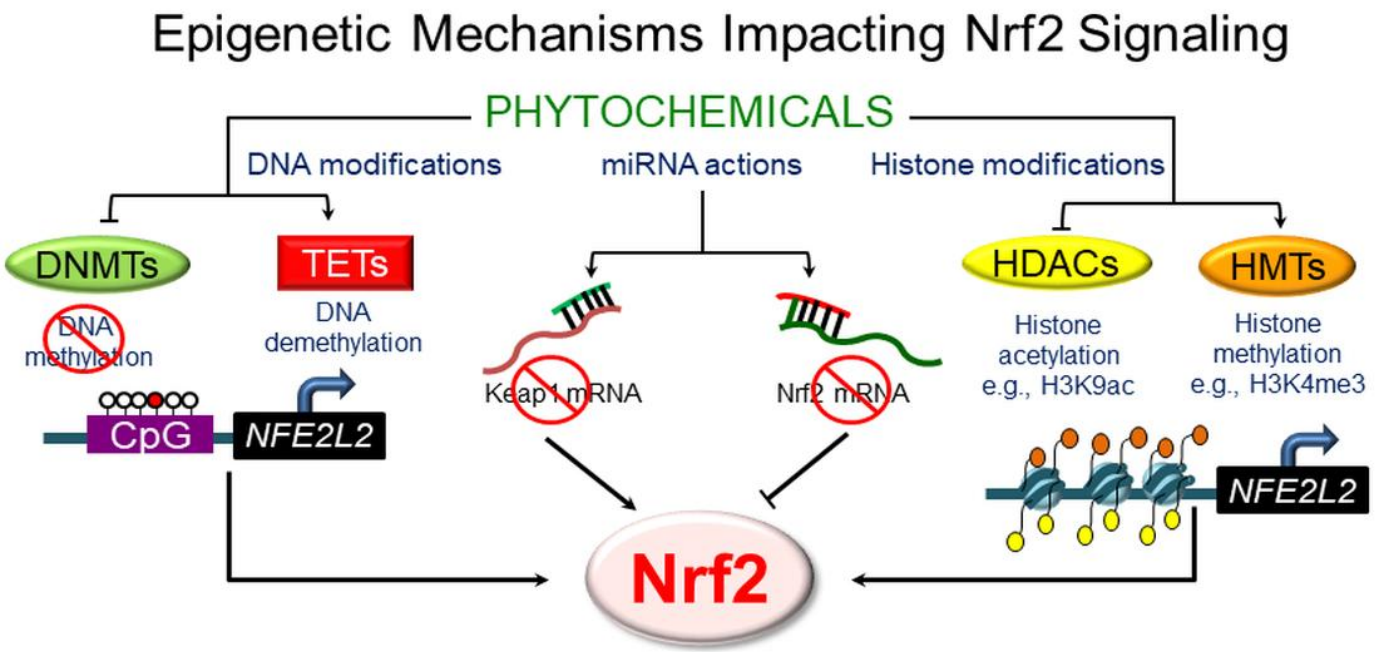
Promotor CpG methylation

Histones

DNA - packaging

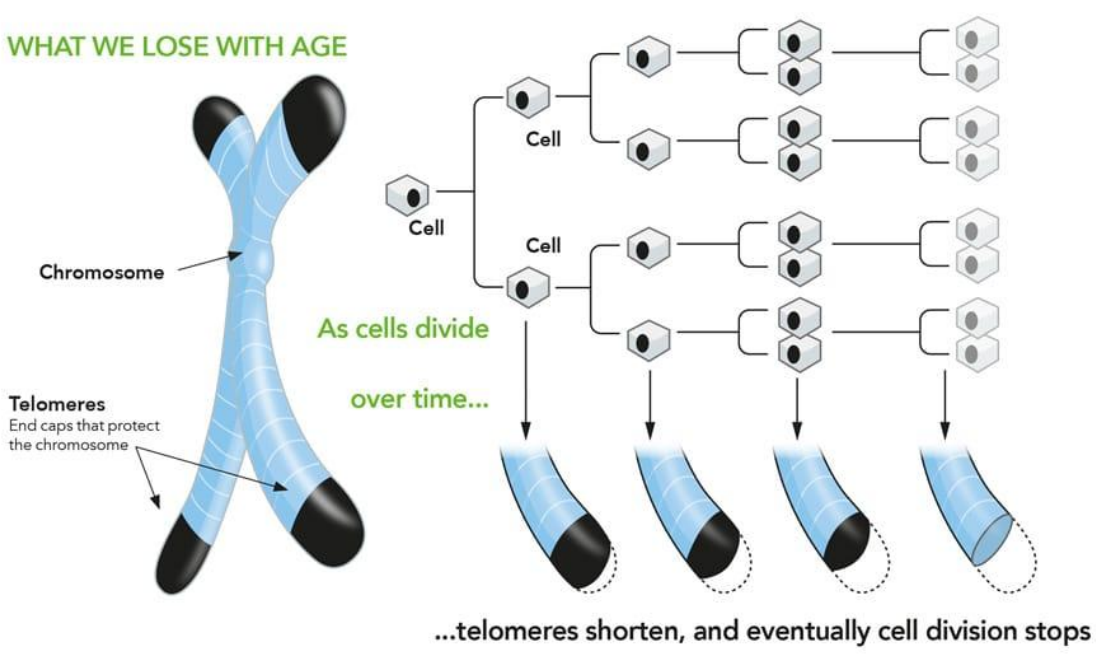
Non-coding miRNAs

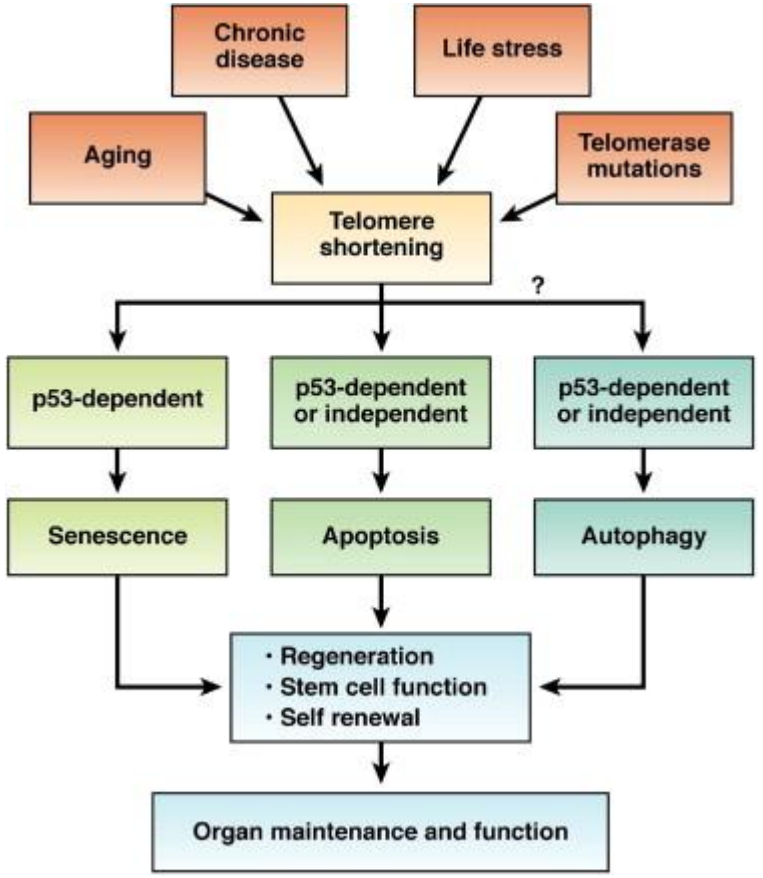
Nutrazeutika, Epigenetik und anti-oxydative Abwehr



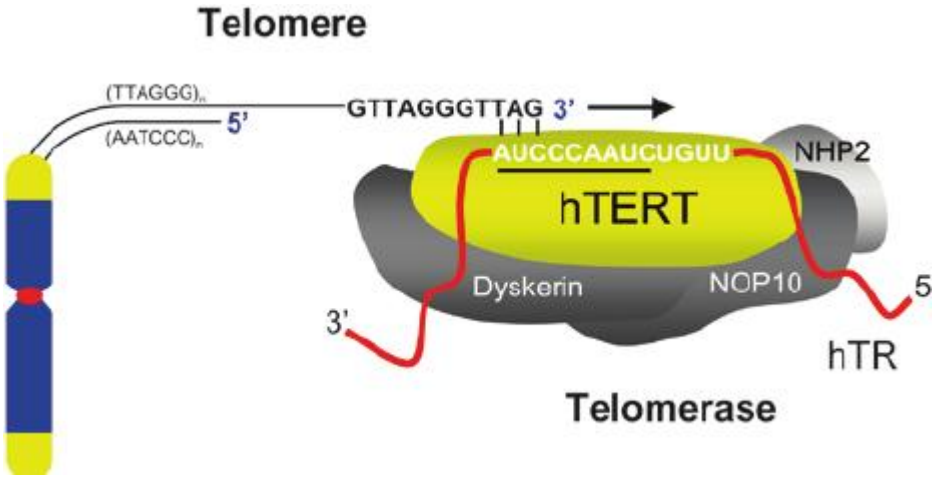
Nrf2 (Nuclear factor erythroid 2-related factor 2) ist ein Transkriptionsfaktor, der eine entscheidende Rolle bei der Regulierung zellulärer Reaktionen auf oxidativen Stress und andere Formen von Zellschäden spielt. Er ist ein wichtiger Regulator des körpereigenen antioxidativen Abwehrsystems.

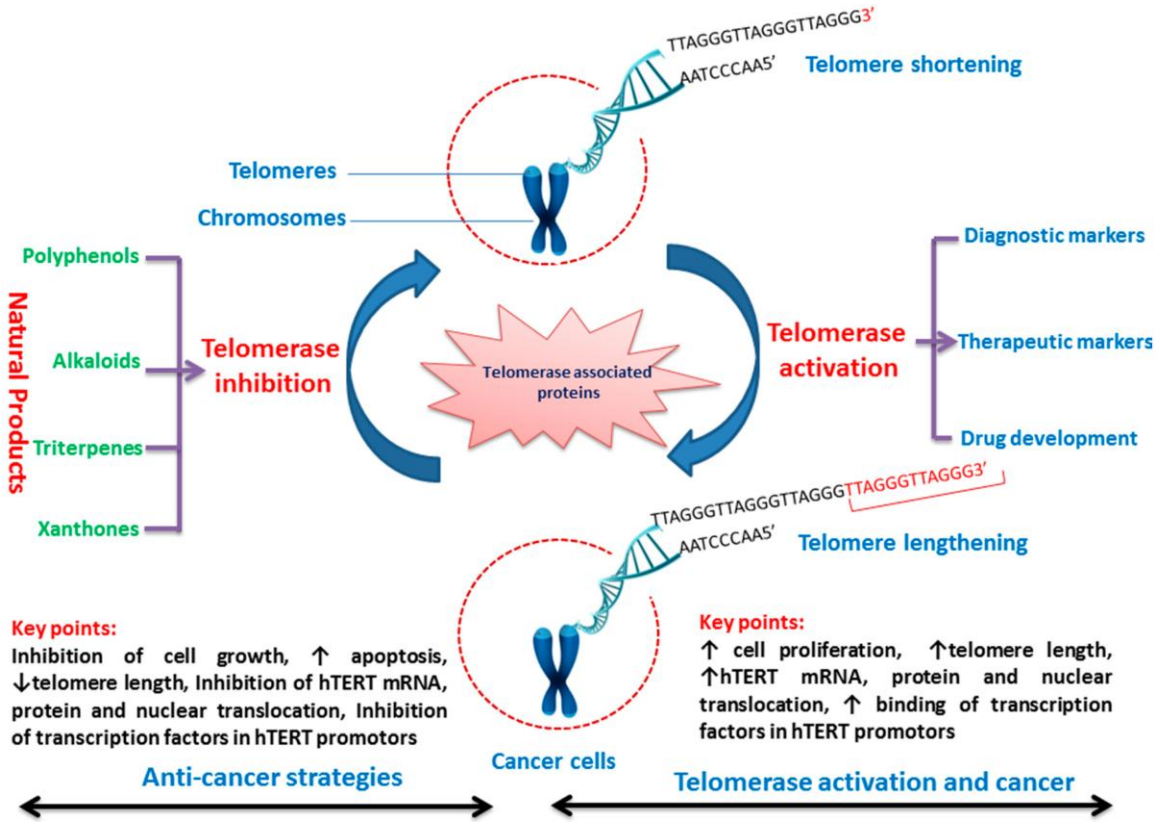
Telomer Verkürzung



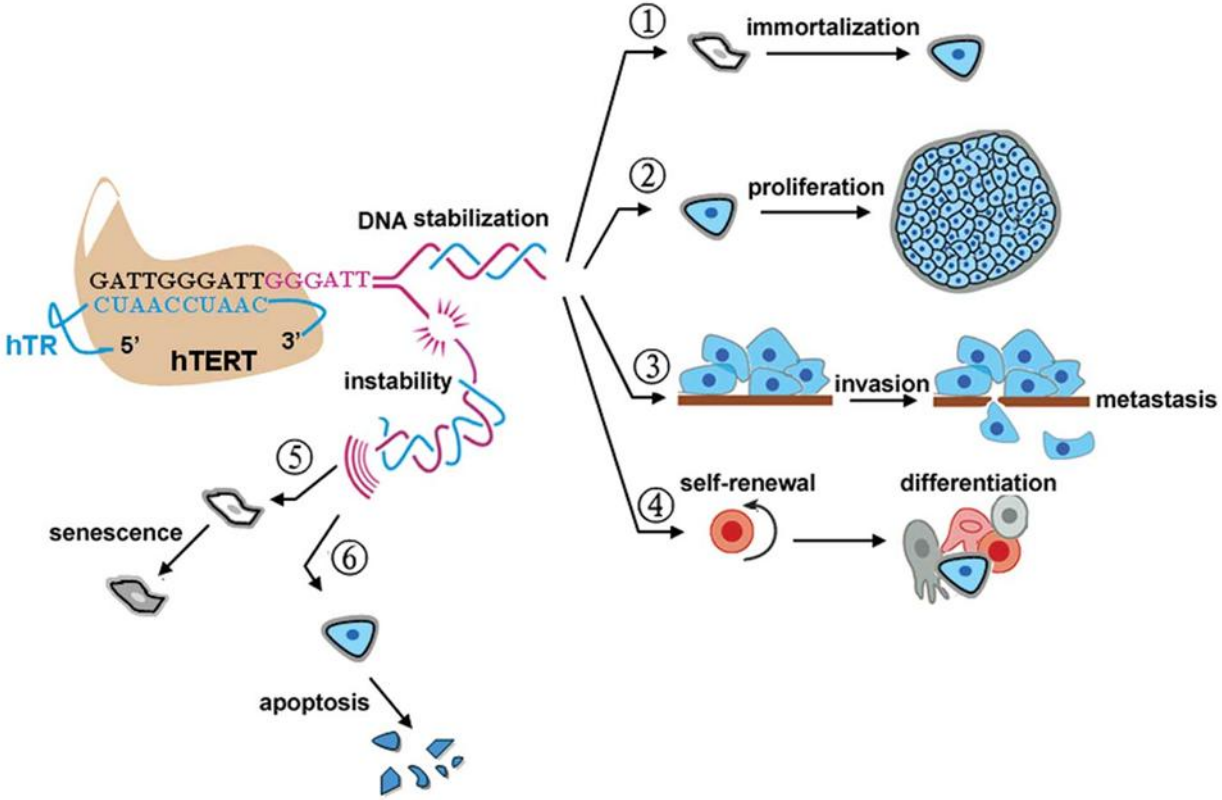


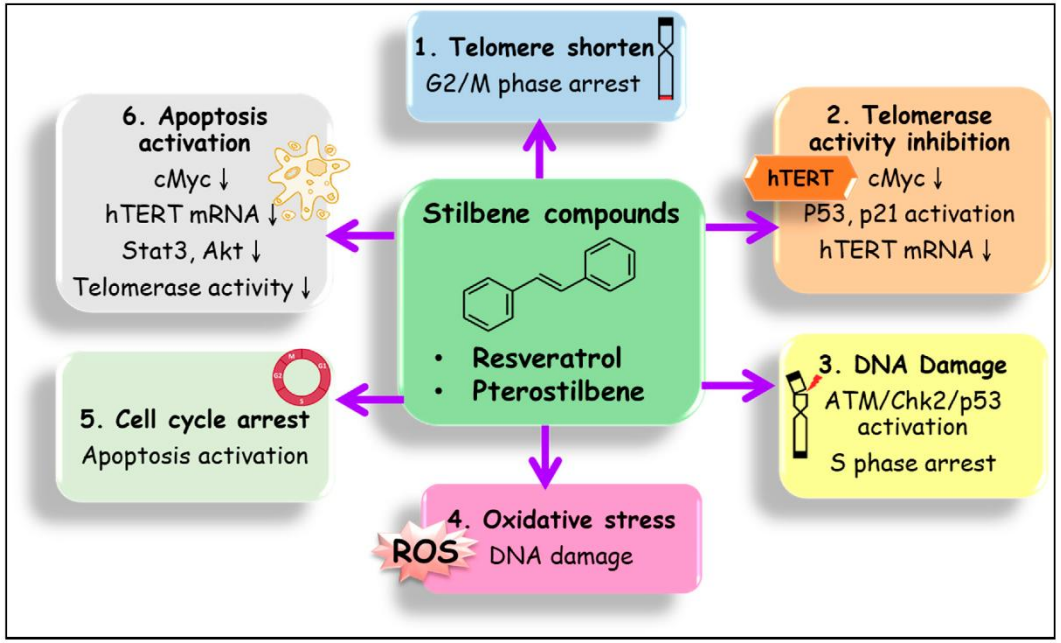
Telomere, telomerase





Polyphenole in der Regulierung von Telomerase, hTERT





EGCG, telomerase, cmyc, hTERT

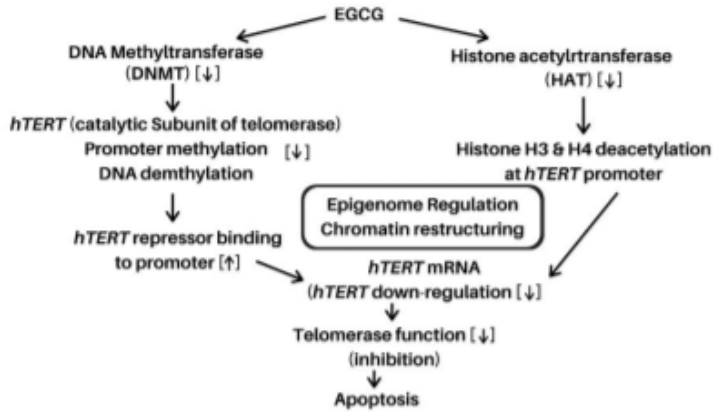
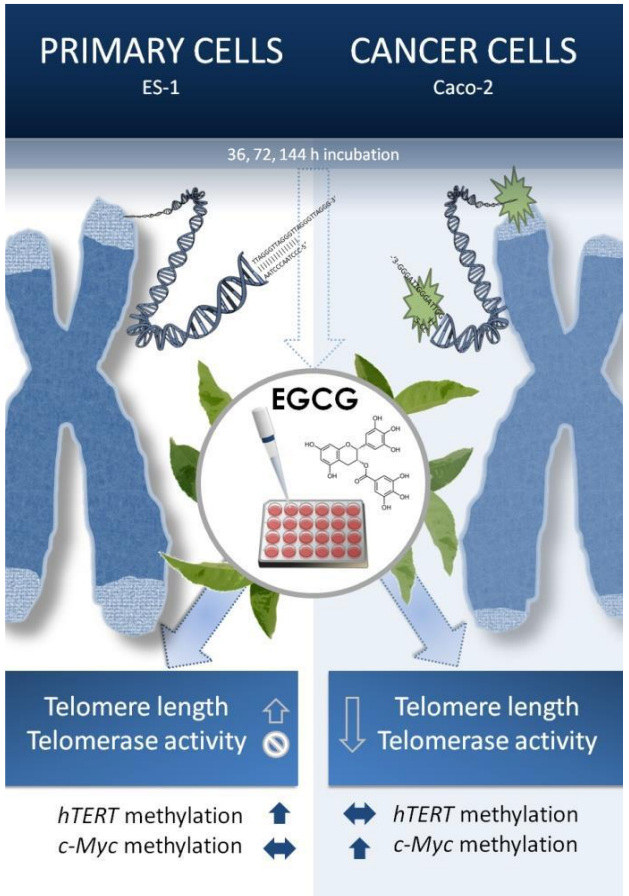


Figure 12. Mechanism of EGCG-induced apoptosis in cancer cells through epigenetic regulation of telomerase. EGCG inhibits both deoxyribonucleic acid (DNA) methyltransferase (DNMT) and histone acetyltransferase (HAT), leading to the DNA demethylation and histones H3 and H4 deacetylation of the

Page | 168

Functional Food and Healthy Aging **First Edition**

human telomerase– reverse transcriptase (hTERT) promoter, respectively. These events result in the epige-

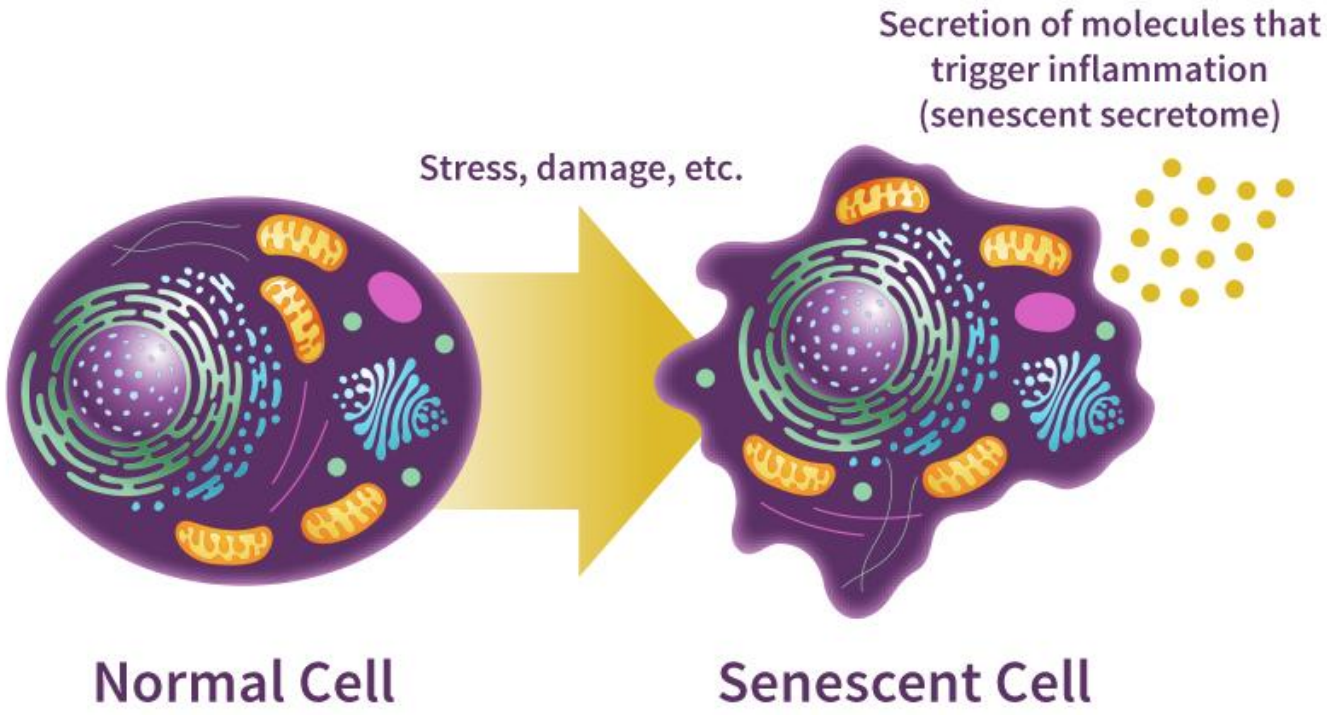


FFHD
Functional Foods in Health and Disease

The green tea polyphenol EGCG is differentially associated with telomeric regulation in normal human fibroblasts versus cancer cells

Angelika Pointner[1], Christine Mölzer[1,2], Ulrich Magnet[1], Katja Zappe[1,3], Berit Hippe[1], Anela Tosevska[1,4], Elena Tomeva[1], Elisabeth Dum[1], Stephanie Lilja[1], Ulrike Krammer[1], Alexander

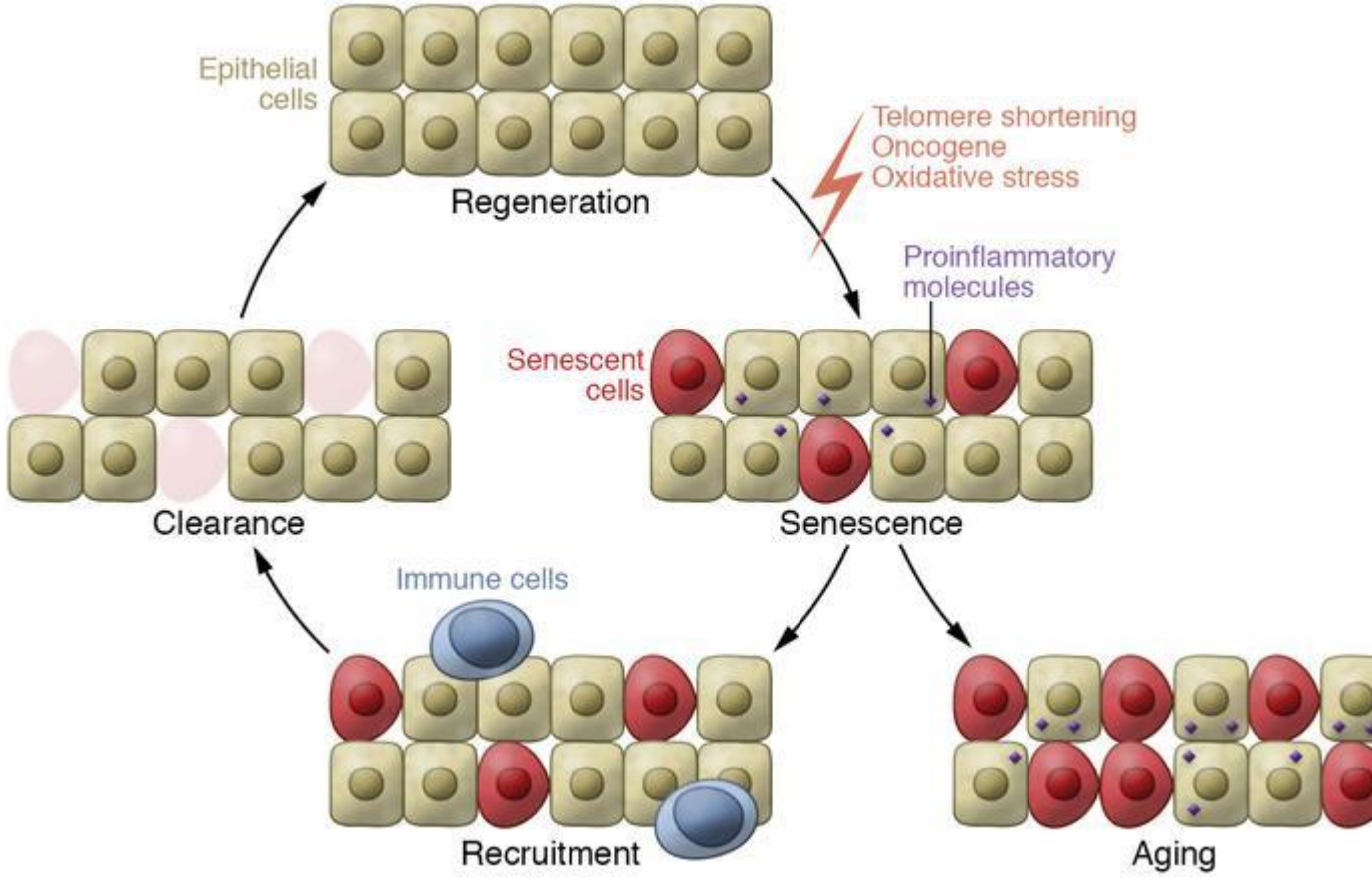
Zelluläre Seneszenz und Polyphenole



Senolytica zwischen Gewebeverjüngung und Krebsprävention

Table 1. Polyphenols and polyphenol derivatives as cancer cell senescence inducers and their effect c

Classification	Compounds	Concentration	Pathways
Resveratrol and its derivatives	Resveratrol	25/50 (μM)	p53/CXCR2
		50 (μM)	BRCA1/DDR
		30 (μM)	ROS/DDR
		100 (μM)	ROS/DLC1/SASP
		6/20 (μM) 100 (μM)	Histone H2B Pokemon
		25/50 (μM)	SIRT1
		50 (μM)	Rictor/RhoA-GTPase
	Pterostilbene	2.5/5/50 (μM)	hTERT/DDR
	Pauciflorol B	10 (μM)	p16/Rb
	3,3′,4,4′-tetrahydroxy-trans-stilbene	10/50/100 (μM)	ROS DDR
Flavonoids	Quercetin	50/100/200 (μM)	RAS/MAPK/ERK PI3K/AKT
	Beta-naphthoflavone	10 (μM)	PI3K/AKT/cyclinD1/D3 MAPK/ERK
	Baicalin	10/20/40 (μM)	DEPP/RAS/Raf/MEK/ERK DEPP/p16/Rb
	IdB 1016	63.2/126.5 (μg/mL)	HER-2/neu p53
	Diosmin	5/10 (μM)	ROS DDR
	Apigenin	Above 25 (μM)	ROS/RNS p16/cyclin D1/p-Rb p21/cyclin E/p-Rb
	Coumestrol	50 (μM)	CKII/ROS/p53/p21
	Rotenone	0.4 (μM)	Ca^{2+}/ROS
	Epigallocatechin gallate	10 (μM)	DDR
	Oroxin A	5/10/15/20 (μM)	p38/ER stress
	Cristacarpin	1 (μM)	p38/ER stress/ROS/p21
	Flavokawain B	3 (μg/mL)	ATF4/DDIT3/TRIB3/AkT/mTOR



Seneszenz und Polyphenole

Hindawi
Oxidative Medicine and Cellular Longevity
Volume 2020, Article ID 4793125, 13 pages
https://doi.org/10.1155/2020/4793125

Hindawi

Research Article

Epigallocatechin Gallate Effectively Affects Senescence and Anti-SASP via *SIRT3* in 3T3-L1 Preadipocytes in Comparison with Other Bioactive Substances

Stephanie Lilja,[1] Julia Oldenburg,[1] Angelika Pointner,[1] Laura Dewald,[1] Mariam Lerch,[1] Berit Hippe,[2] Olivier Switzeny,[2] and Alexander Haslberger[1]

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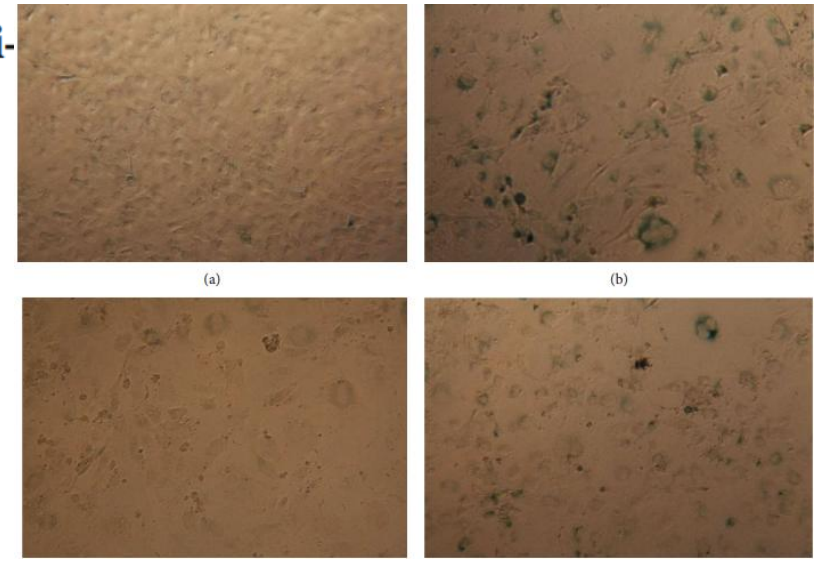
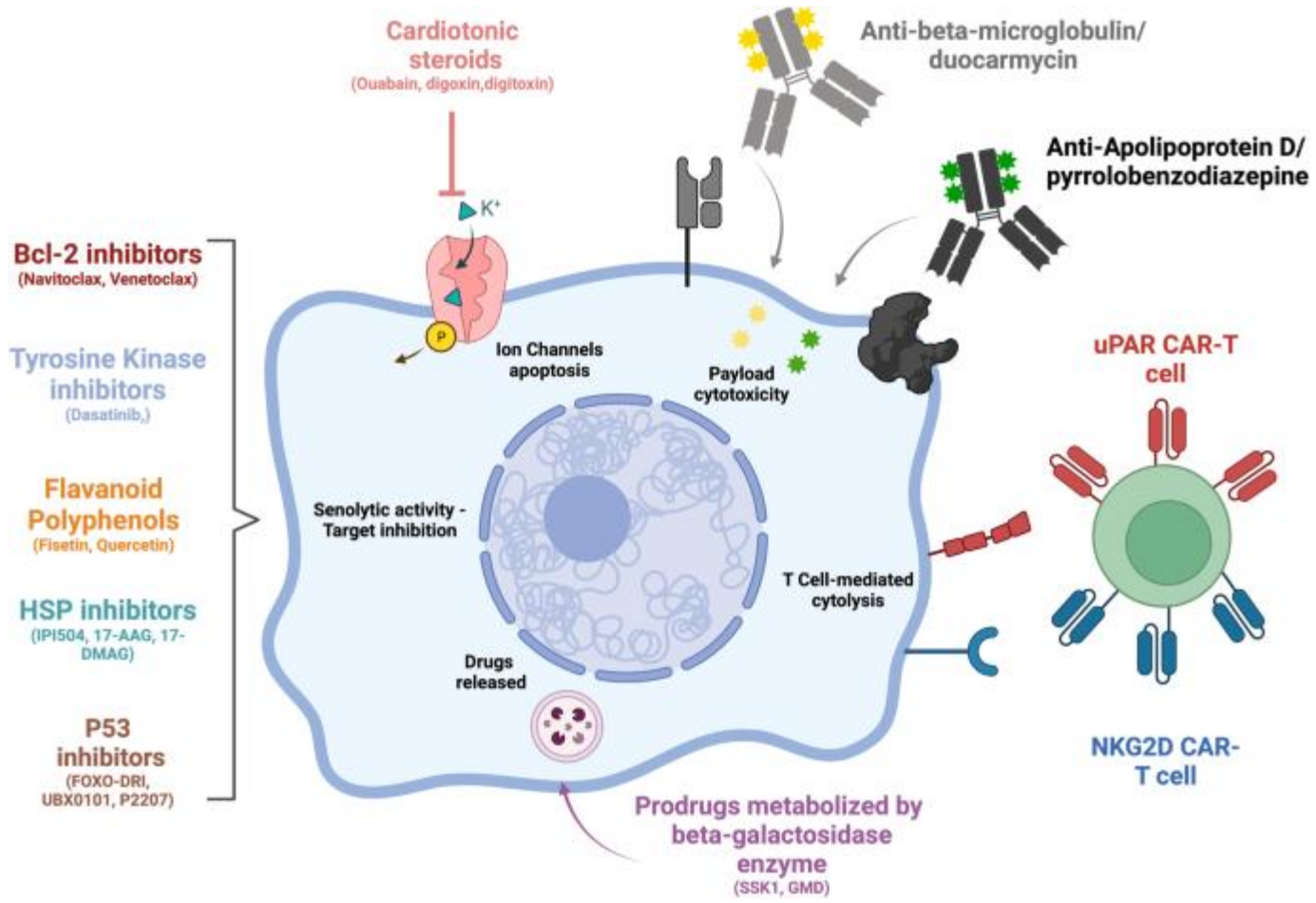


Senolytics_ Millionen $ Märkte



Mausstudie: EGCG reduzierte durch fettreiche Ernährung induzierte Strangbrüche, DNMt1, Comet-Assay

Hindawi
Oxidative Medicine and Cellular Longevity
Volume 2017, Article ID 3079148, 17 pages
https://doi.org/10.1155/2017/3079148

Hindawi

Research Article

EGCG Prevents High Fat Diet-Induced Changes in Gut Microbiota, Decreases of DNA Strand Breaks, and Changes in Expression and DNA Methylation of *Dnmt1* and *MLH1* in C57BL/6J Male Mice

Marlene Remely,[1] Franziska Ferk,[2] Sonja Sterneder,[1] Tahereh Setayesh,[2] Sylvia Roth,[1] Tatjana Kepcija,[1] Rahil Noorizadeh,[2] Irene Rebhan,[1] Martina Greunz,[1] Johanna Beckmann,[1] Karl-Heinz Wagner,[1] Siegfried Knasmüller,[2] and Alexander G. Haslberger[1]

European Journal of Nutrition
https://doi.org/10.1007/s00394-018-1782-2

ORIGINAL CONTRIBUTION

CrossMark

Gallic acid, a common dietary phenolic protects against high fat diet induced DNA damage

Tahereh Setayesh[1] · Armen Nersesyan[1] · Miroslav Mišík[1] · Rahil Noorizadeh[1,3] · Elisabeth Haslinger[1] · Tahereh Javaheri[2,3] · Elisabeth Lang[1] · Michael Grusch[1] · Wolfgang Huber[1] · Alexander Haslberger[4] · Siegfried Knasmüller[1]

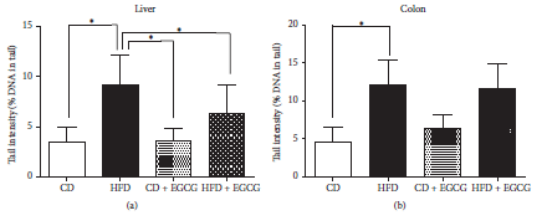


FIGURE 3: Impact of EGCG supplementation on DNA damage in liver (a) and colon (b) of C57BL/6J male mice. Bars indicate means ± SD of results obtained with 15 animals per group. From each sample, three slides were made and 50 cells were evaluated per slide (CD = control diet, HFD = high fat diet, and CD + EGCG = control diet plus EGCG; HFD + EGCG = high fat diet plus EGCG; stars indicate significance: $^{*}p$ value ≤ 0.05).

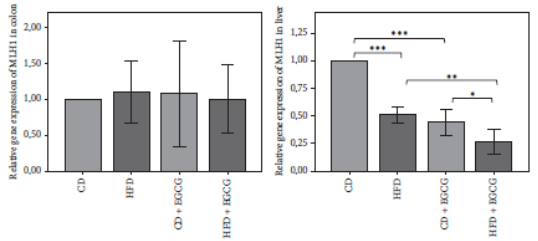
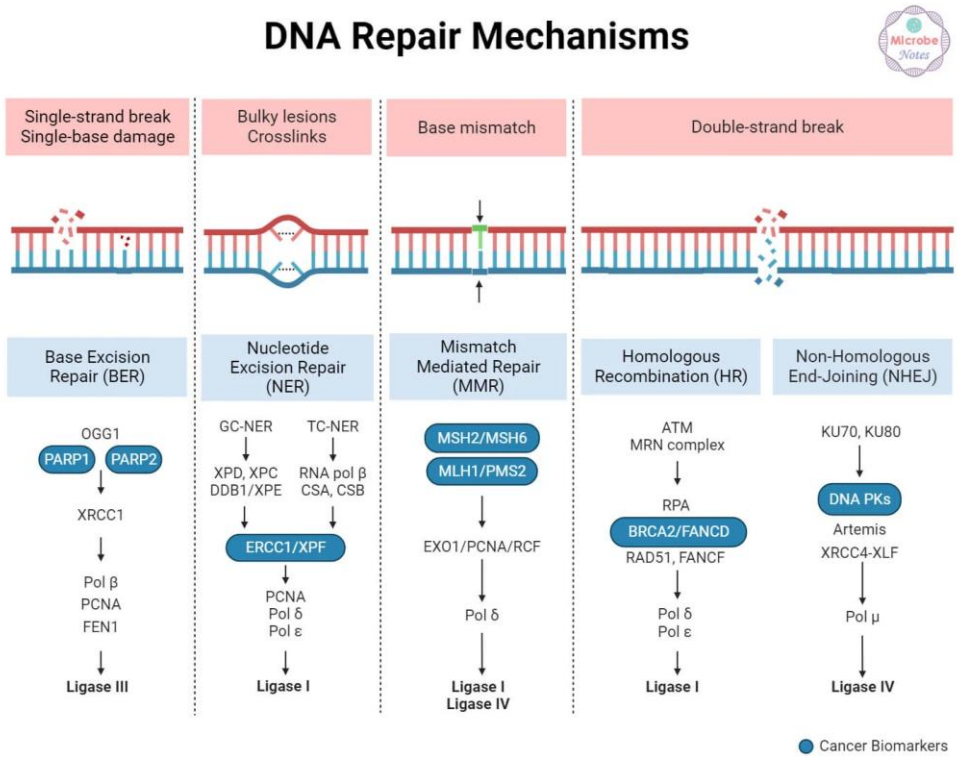
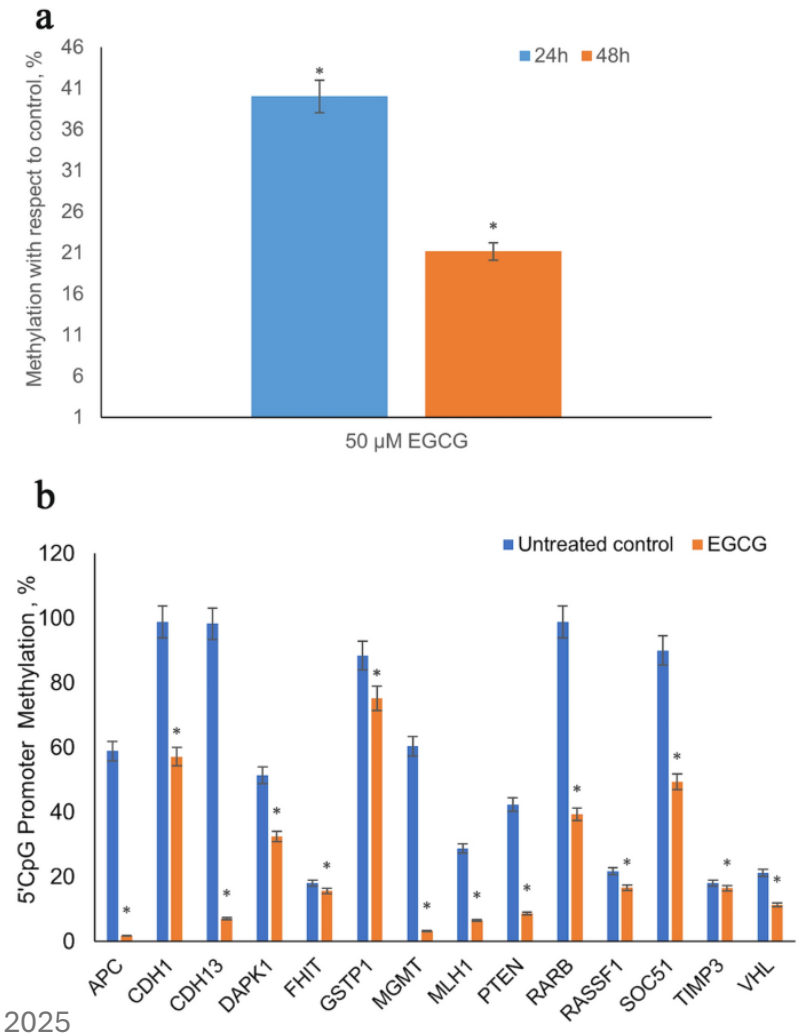


FIGURE 4: Relative gene expression of *MLH1* in colon (a) and liver (b) of C57BL/6J male mice. All gene expression data are relative to CD and were normalized to the house keeping gene *GAPDH*. Error bars represent 95% confidence intervals (CD = control diet, HFD = high fat diet, and CD + EGCG = control diet plus EGCG; HFD + EGCG = high fat diet plus EGCG; stars indicate significance: $^{*}p$ value ≤ 0.05, $^{**}p$ value ≤ 0.01, and $^{***}p$ value ≤ 0.001).

EGCG und MGMT and MLH1 DNA repair enymes and promotor methylation, mouse





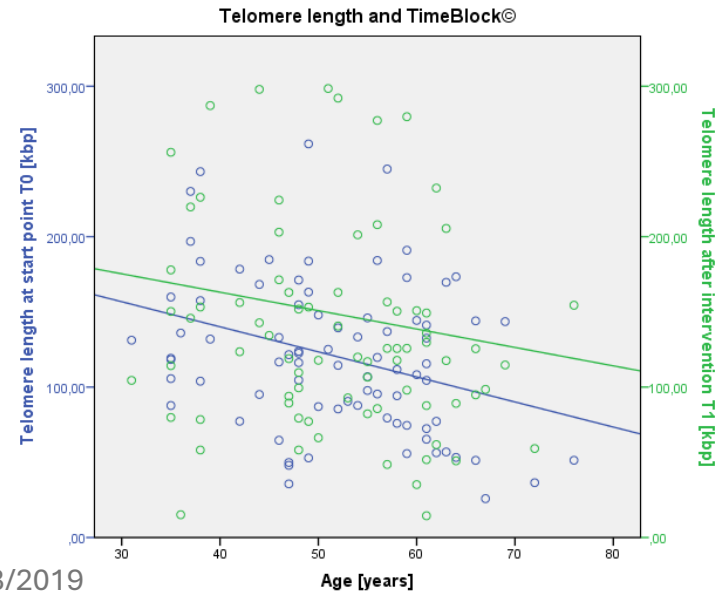
Additiva, Qualität und Dosis: Timeblock® increase telomere length and improves epigenetic markers

Journal of Nutrition & Food Sciences
ISSN: 2155-9600
Pointner et al., J Nutr Food Sci 2017, 7:1
DOI: 10.4172/2155-9600.1000577
Research Article
OMICS International

EGCG Containing Combined Dietary Supplement Affects Telomeres and Epigenetic Regulation

Angelika Pointner, Ulrich Magnet, Elena Tomeva, Elisabeth Dum, Christina Bruckmueller, Christine Mayer, Eva Aumueller and Alexander Haslberger*

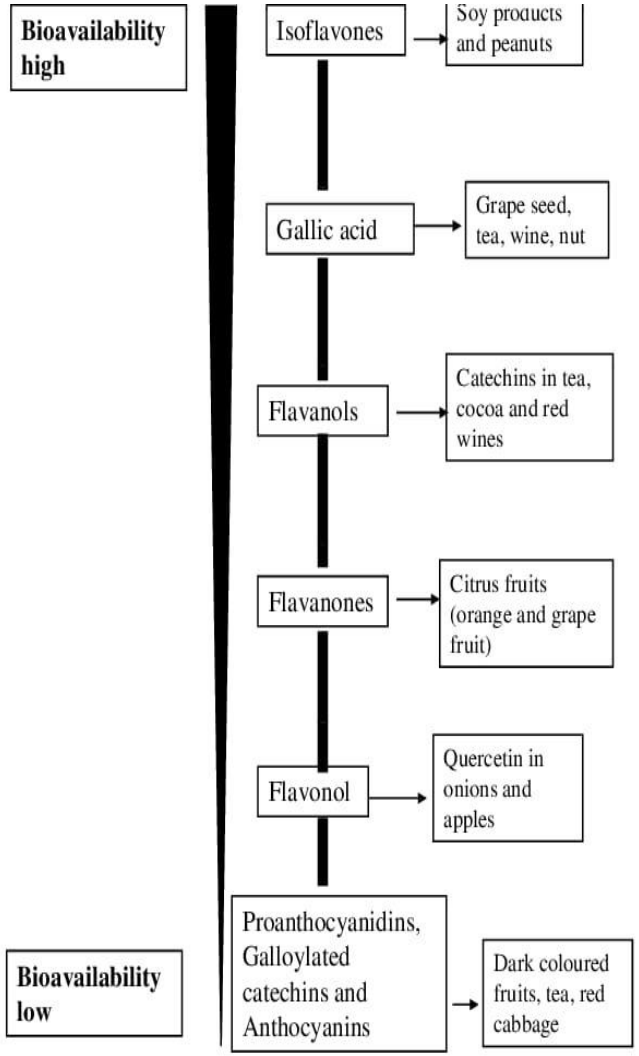
Department of Nutritional Sciences, University of Vienna, Austria

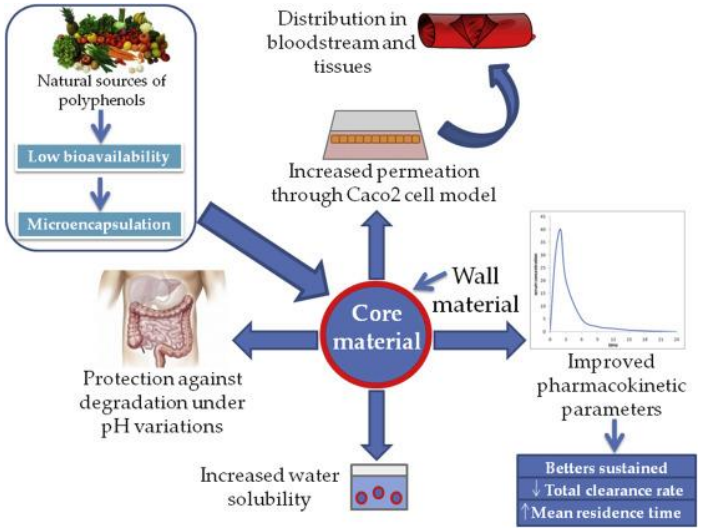


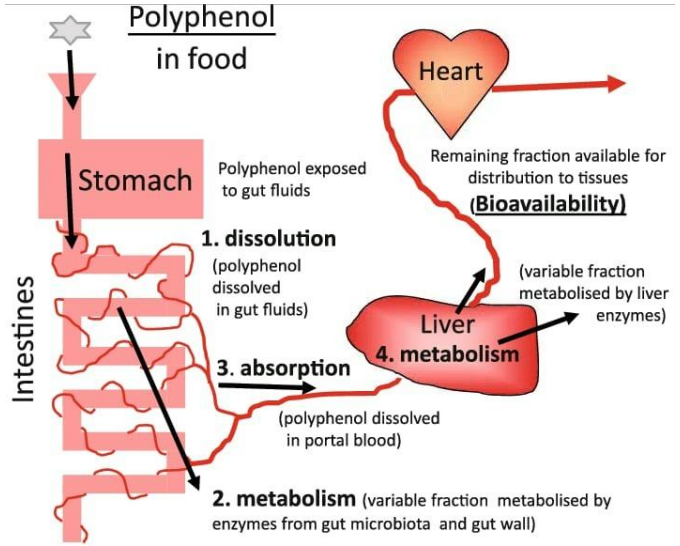
- **Green Tea Tips:** Provides antioxidants like Epigallocatechin Gallate
- **Barley Grass and Wheatgrass:** Sources of nutrients and antioxidants.
- **Algae:** Rich in nutrients and antioxidants.
- **Grape Seeds:** A source of antioxidants.
- **Shiitake Mushrooms:** Provide nutrients.
- **Tomatoes and Marigold:** Contribute nutrients and antioxidants.
- **Vitamin C:** Supports cell division.
- **Zinc:** An essential mineral.
- **Selenium:** An essential mineral.
- **Equol:** A phytoestrogen with potential benefits for skin aging.
- **Epigallocatechin Gallate:** An antioxidant from green tea.
- **Pyrroloquinoline quinone (PQQ):** An antioxidant that protects against mitochondrial damage.

Barley grass juice powder grown Bhutan
Wheat grass sprout powder -grown Bhutan
Green tea leaf extract(grown Japan)
Pro Kapsel etwa 200 mg EGCG (50 % des Catechins), was ca. 5 Tassen Grüntee entspricht

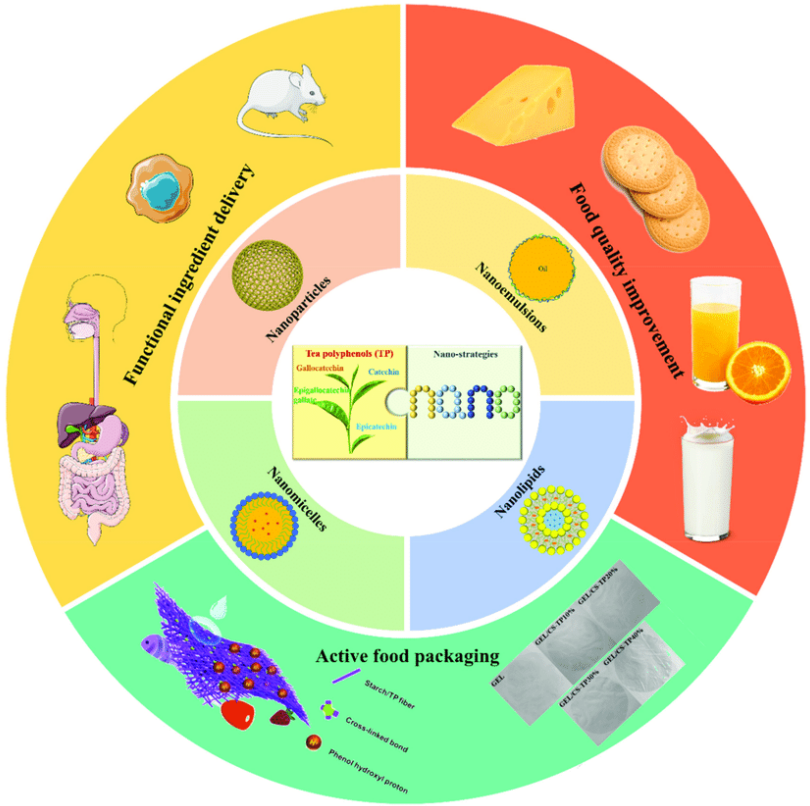
Aber: Polyphenole Bioverfügbarkeit, Stabilitaet

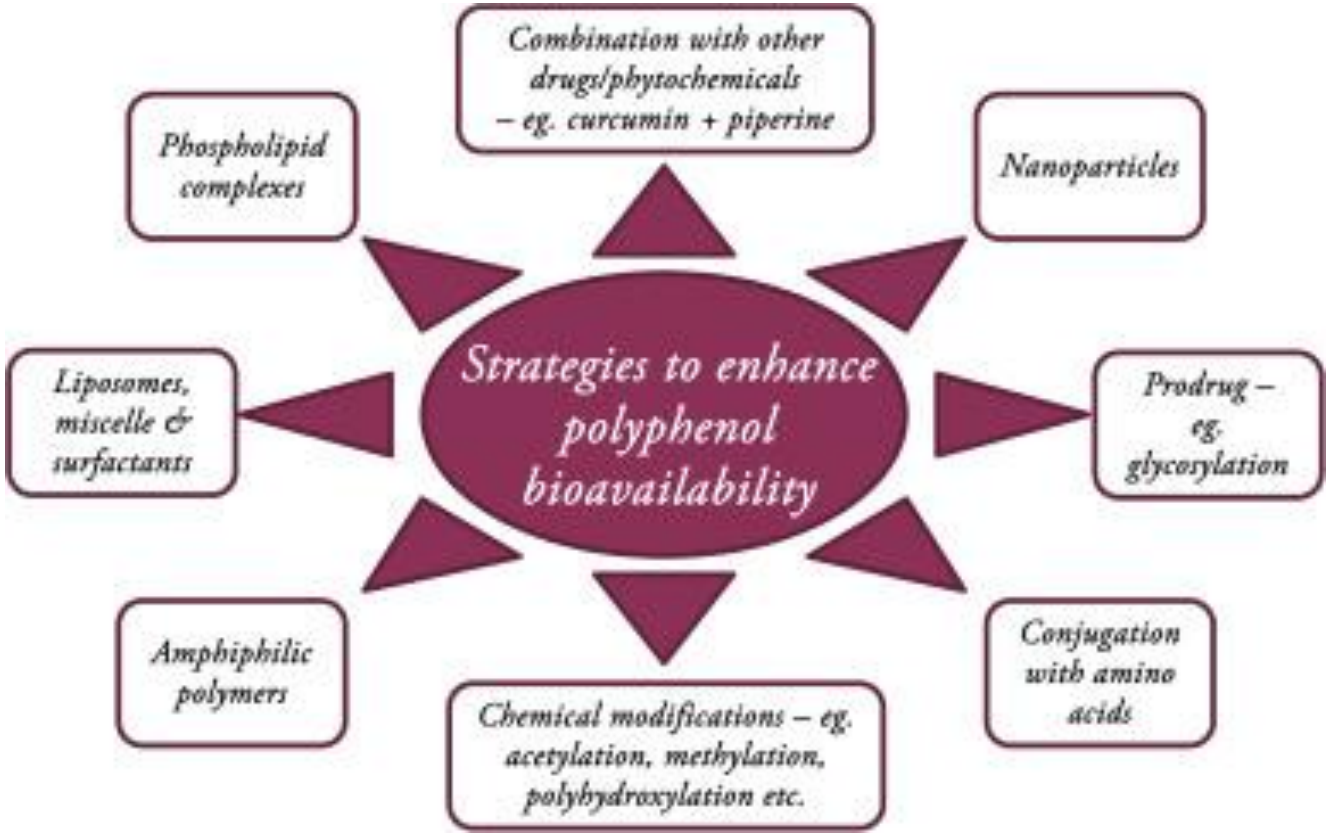




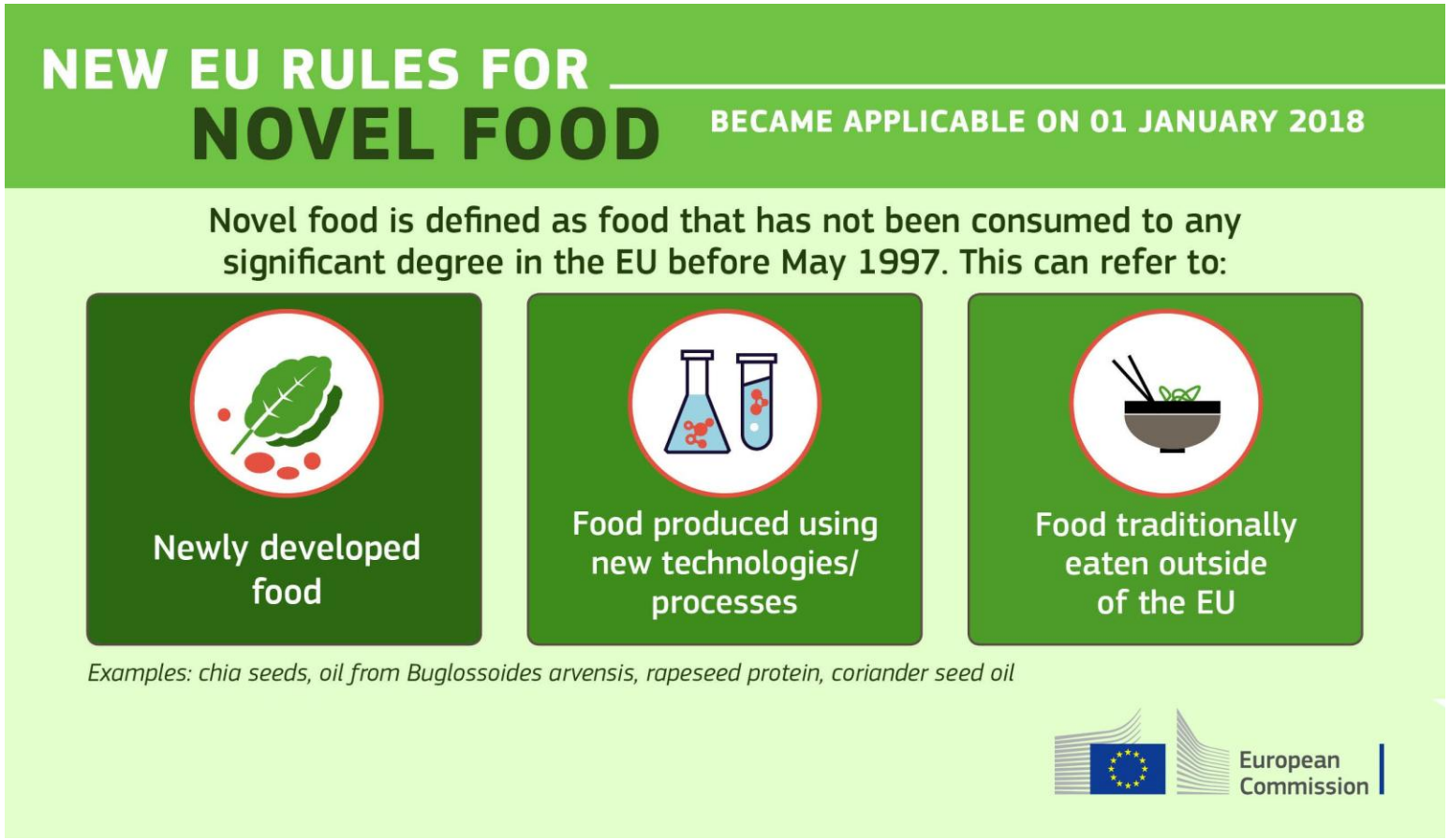


Verbesserung der Stabilität von Polyphenolen, Liposomen, Nanopartikeln, novel food





Vorschriften und tolerierbare obere Aufnahmemenge"die maximale tägliche Aufnahme eines Nährstoffs, bei der es unwahrscheinlich ist, dass sie negative Auswirkungen auf die Gesundheit hat



Novel Food" am Markt bezieht sich auf neuartige Lebensmittel, die in der Europäischen Union erst seit dem 15. Mai 1997 in nennenswertem Umfang für den menschlichen Verzehr verwendet wurden

The EFSA ANS Panel was asked to provide a scientific opinion on the safety of green tea catechins from dietary sources including preparations such as food supplements and infusions. Green tea is produced from the leaves of Camellia sinensis (L.) Kuntze, without fermentation, which prevents the oxidation of polyphenolic components. Most of the polyphenols in green tea are catechins. The Panel considered the possible association between the consumption of (-)-epigallocatechin-3-gallate (EGCG), the most relevant catechin in green tea, and hepatotoxicity. This scientific opinion is based on published scientific literature, including interventional studies, monographs and reports by national and international authorities and data received following a public 'Call for data'. The mean daily intake of EGCG resulting from the consumption of green tea infusions ranges from 90 to 300 mg/day while exposure by high-level consumers is estimated to be up to 866 mg EGCG/day, in the adult population in the EU. Food supplements containing green tea catechins provide a daily dose of EGCG in the range of 5–1,000 mg/day, for adult population. The Panel concluded that catechins from green tea infusion, prepared in a traditional way, and reconstituted drinks with an equivalent composition to traditional green tea infusions, are in general considered to be safe according to the presumption of safety approach provided the intake corresponds to reported intakes in European Member States. However, rare cases of liver injury have been reported after consumption of green tea infusions, most probably due to an idiosyncratic reaction. Based on the available data on the potential adverse effects of green tea catechins on the liver, the Panel concluded that there is evidence from interventional clinical trials that intake of doses equal or above 800 mg EGCG/day taken as a food supplement has been shown to induce a statistically significant increase of serum transaminases in treated subjects compared to control.

The logic of maxium intake doses:

Lifetime consumption:

periodical consumption?

Herstellung: Wege um die Zulassung nach Novel food Regulation zu vermeiden, zb Spermidin

Vorabentscheidungsersuchen des LG Graz, Rechtssache C-141/22 – Auslegungsfragen zur Novel-Food-Verordnung / Thema Spermidin.

Das VerfahreHern betrifft ein Nahrungsergänzungsmittel mit Spermidin, bei welchem bei der Herstellung des Produkts Buchweizensaat in eine Näle synthetisches Spermidin enthält, als Hydrokultur zu Sprossen keimt. Nach der Ernte wird der Keimling mit Wasser gewaschen, getrocknet und zu Keimlingsmehl vermahlen. Durch die Herstellung entstehen nicht mehr Keimlinge als Saatkörner eingesetzt werden. Der Spermidingehalt des Buchweizenkeimlingsmehls beträgt 3,5 mg pro Gramm.

Das Gericht hat folgende Fragen dem EuGH vorgelegt:

1) Ist Art. 3 Abs. 2 Buchst. a Ziffer iv) der Verordnung (EU) 2015/2283 so auszulegen, dass „Buchweizenkeimlingsmehl mit hohem Spermidingehalt" ein neuartiges Lebensmittel darstellt, sofern nur Buchweizenkeimlingsmehl mit einem nicht erhöhten Spermidingehalt vor dem 15.5.1997 in nennenswertem Umfang für den menschlichen Verkehr in der Europäischen Union verwendet wurde oder danach eine Verwendungsgeschichte als sicheres Lebensmittel hat, unabhängig davon, wie das Spermidin in das Buchweizenkeimlingsmehl gelangt?

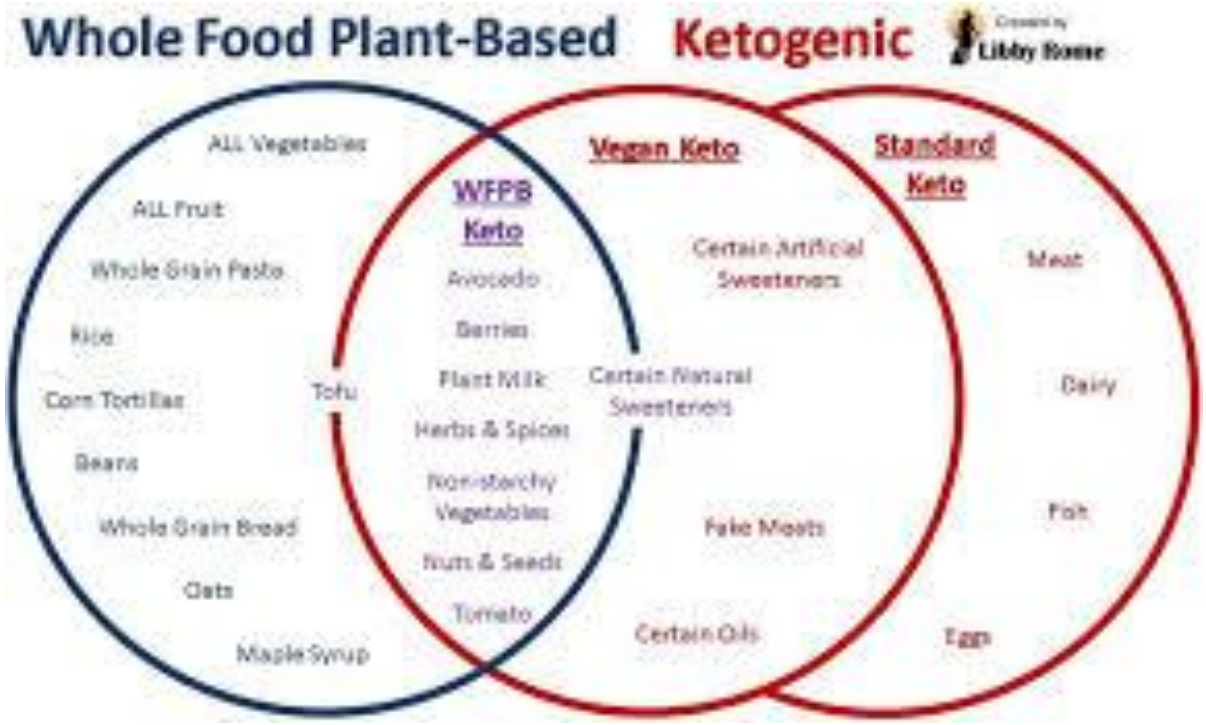
2) Bei Verneinung der Frage 1.: Ist Art. 3 Abs. 2 Buchst. a Ziffer vii) der Verordnung 2015/2283 so auszulegen, dass der Begriff des Herstellungsverfahrens von Lebensmitteln auch Verfahren in der Primärproduktion umfasst?

3) Bei Bejahung der Frage 2.: Kommt es für die Frage der Neuartigkeit eines Herstellungsverfahrens im Sinne des Art. 3 Abs. 2 Buchst. a Ziffer vii) der Verordnung 2015/2283 darauf an, ob das Herstellungsverfahren an sich noch nie bei irgendeinem Lebensmittel oder ob es bei dem zu beurteilenden Lebensmittel nicht angewandt wurde?

4) Bei Verneinung der Frage 2.: Handelt es sich beim Keimen von Buchweizensaat in einer spermidinhaltigen Nährlösung um ein Verfahren der Primärproduktion in Bezug auf eine Pflanze, auf die die lebensmittelrechtlichen Vorschriften, insbesondere die Verordnung 2015/2283, keine Anwendung findet, da die Pflanze vor dem Zeitpunkt der Ernte noch kein Lebensmittel ist (Art. 2 Buchst. c der Verordnung (EG) Nr. 178/2002 (2))?

5) Macht es einen Unterschied, ob die Nährlösung natürliches oder synthetisches Spermidin enthält?

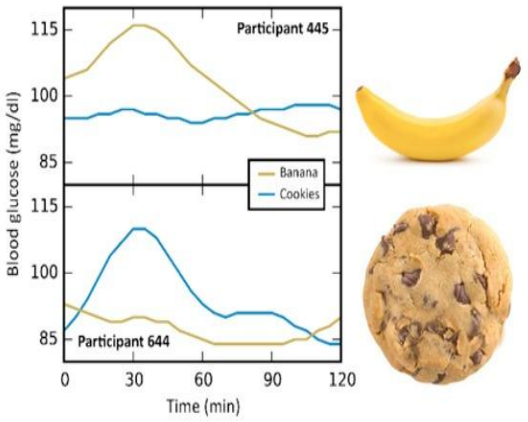
Diet: one size fits all ?

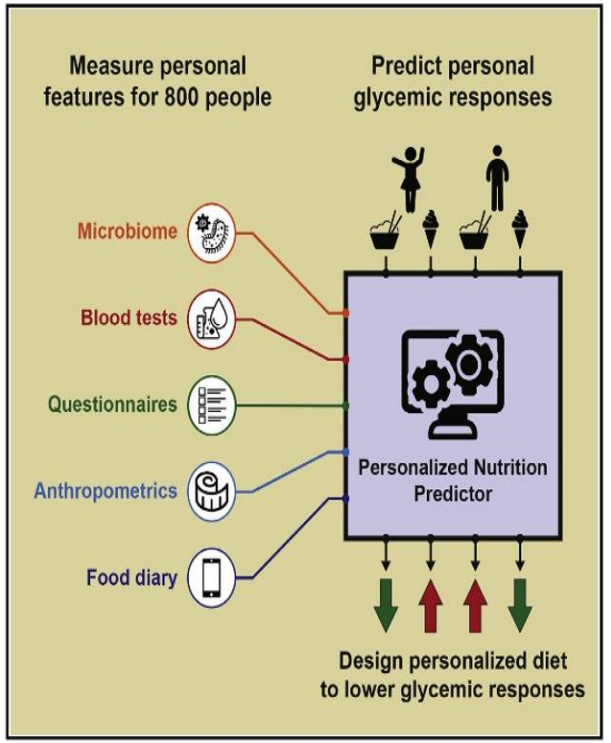


Individuell unterschiedliche glykämische Antworten

Beispiel - Personalized Nutrition by Prediction of Glycemic Responses
David Zeevi, 2016

- 800 Personen – jeder hat andere „post meal Glucose response“





Mikrobiota Zusammensetzung beeinflusst Blutglucoselevel

Alterung, Ageotypen

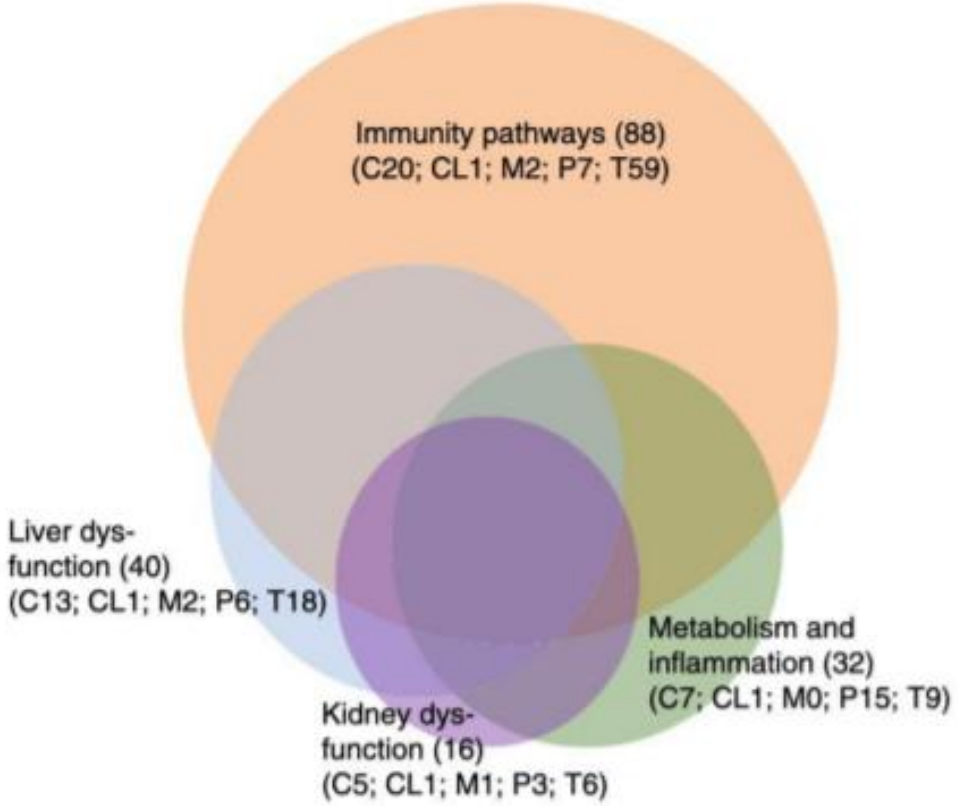


Figure 21. Ageotypes, personalized aging [186]

Ernährungsberatung durch molekulare Marker-Analyse: Genetik, Epigenetik, Mikrobiota, Metabolomik

BIOMES

Erkenntnissen über:

- Darmgesundheit & deinen Darmtyp
- Bakterienvielfalt
- Kalorienaufnahme
- Stärken & Schwachstellen
- Personalisierte Empfehlungen

In den Warenkorb

METWARE BIO Metabolomics Services Applications

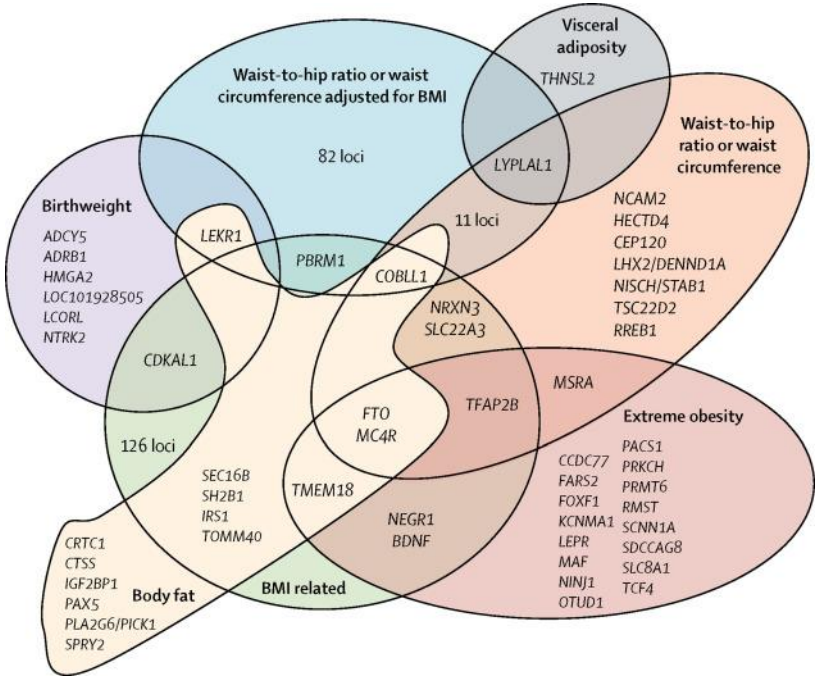
Global Metabolite Profiling >
Targeted Metabolomics >
Lipidomics >
Multi-Omics >

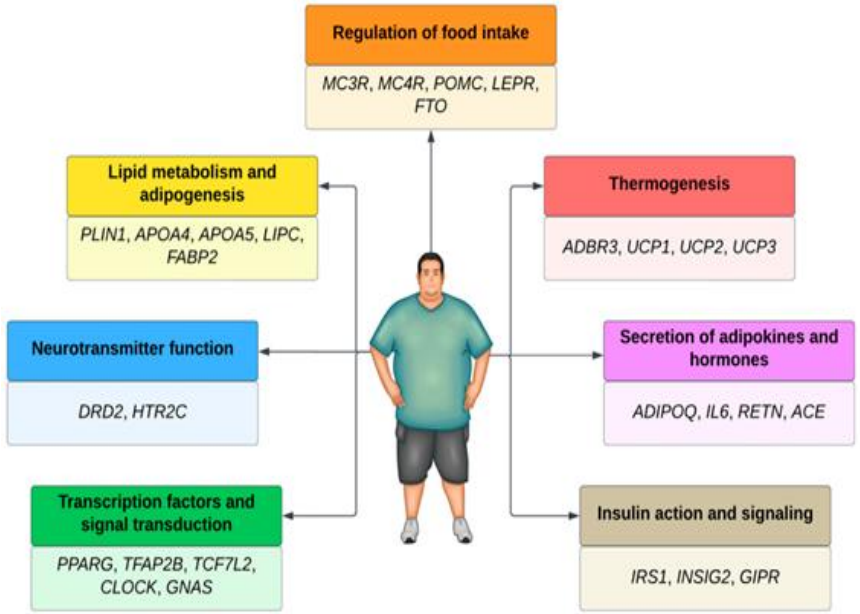
Metware Biotechnology Inc (Metware) is a metabolomics CRO focusing on developing and applying innovative metabolome technologies to life science and health research. With over 40 mass

HealthBioCare GmbH

GENETISCHE UND EPIGENETISCHE ANALYSE
ERNÄHRUNG|

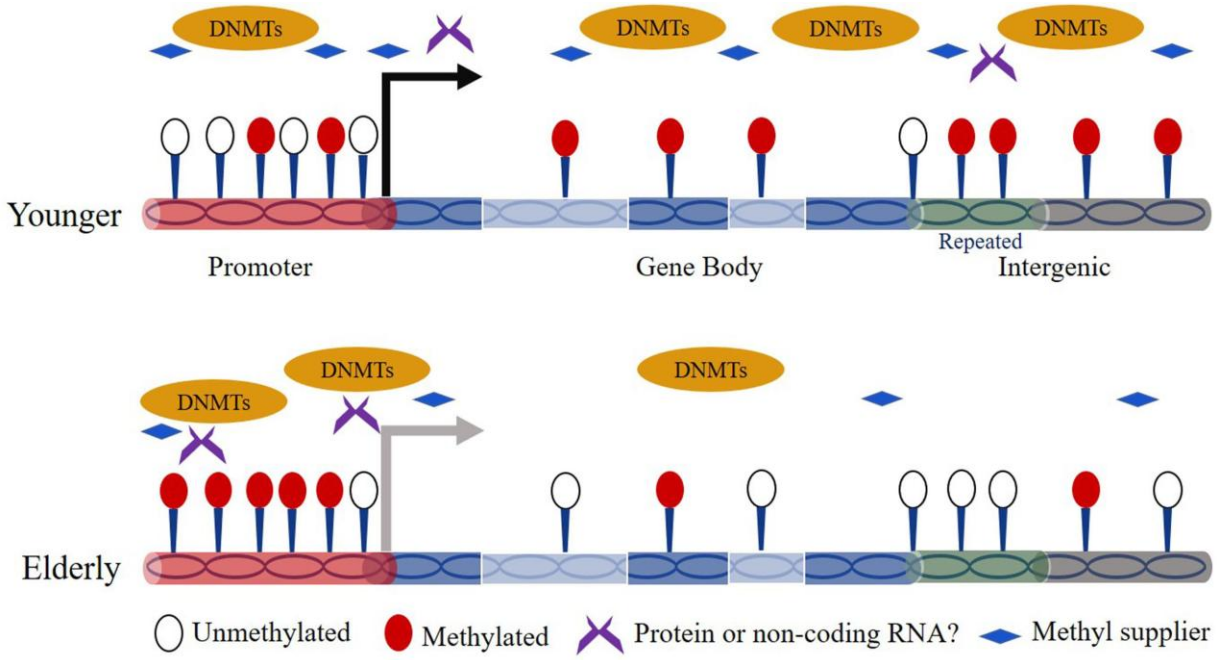
Genetik und reine SNP-Analyse wenig aussagekräftig?

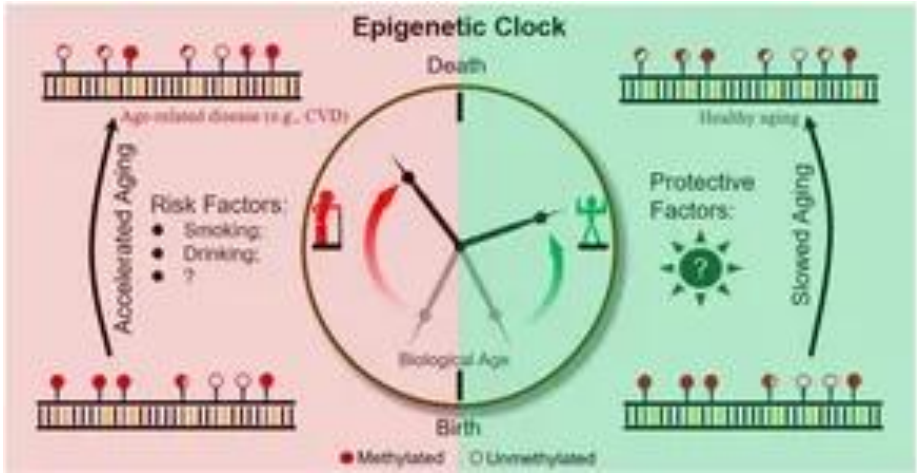




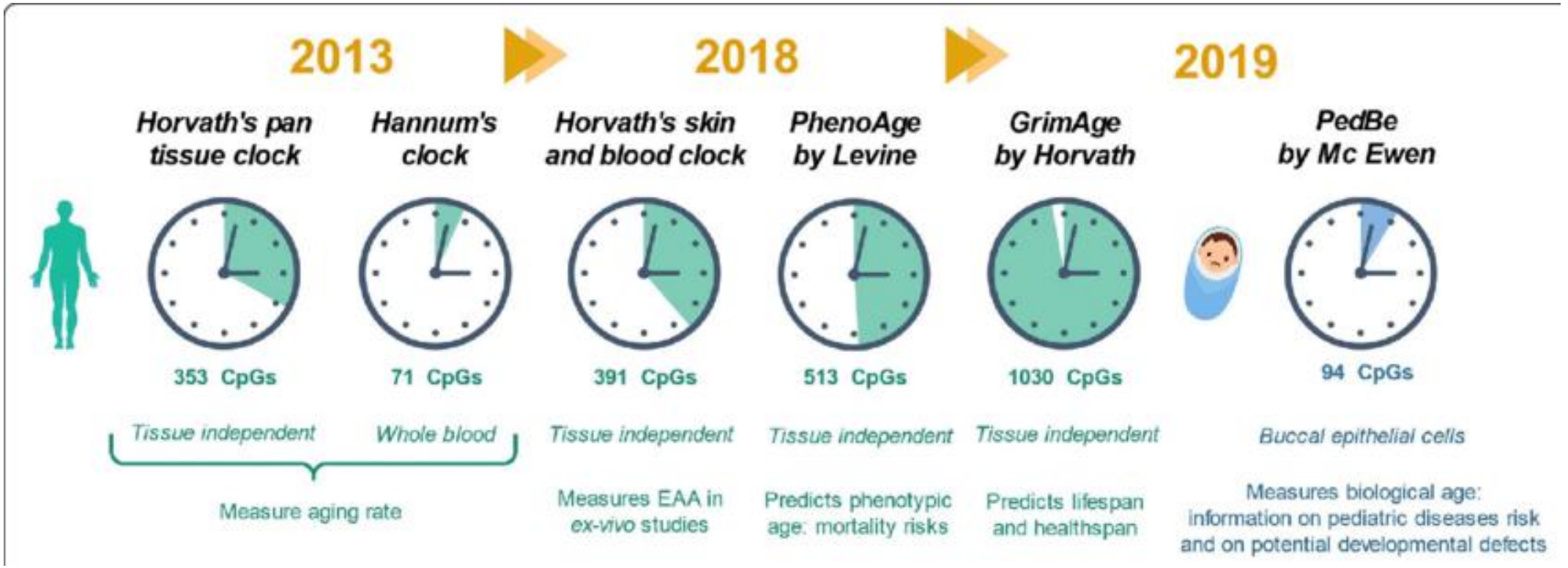
For diseases controlled by 1000 loci of mean relative risk of only 1.04, a case-control study with 10,000 cases and controls can lead to selection of ~75 loci that explain >50% of the genetic variance. The 5% of people with the highest predicted risk are three to seven times more likely to suffer the disease than the population average, depending on heritability and disease prevalence. Whether an individual with known genetic risk develops the disease depends on known and unknown environmental factors.

Epigenetische Methylierungen verändern sich mit dem Alter: ein guter Marker

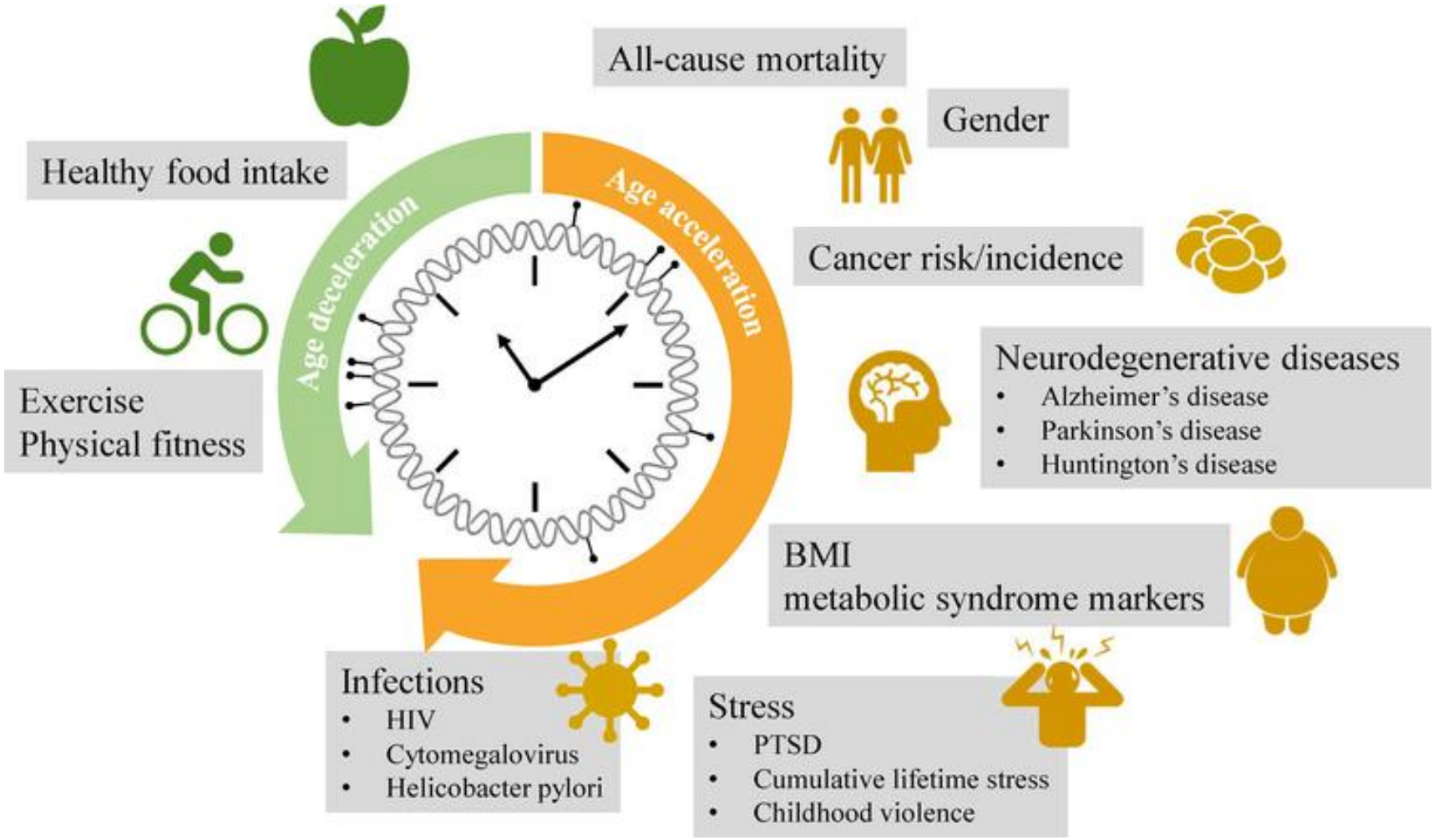




Developments of epigenetic clocks



The epigenetic clock, Horvath



Epigenetic clock based on age related changes of miRNAS: Health Bio Care

frontiers

MiRNA-3 Age: A microRNA-Based Biological Age Model and Its Modulation by Lifestyle and Nutrition

Jana Schneider[†1,2], Clara Preyer[†1,2], Marie Steil[1], Alexander Haslberger[1], Berit Hippe[1,2*]

[1]Department of Nutritional Sciences, University of Vienna, 1090 Vienna, Austria

[2]HealthBioCare GmbH, 1090 Vienna, Austria

*** Correspondence:**
Dr. Berit Hippe
bh@healthbiocare.at

†These authors share first authorship

Keywords: Epigenetics, microRNA, Aging, Nutrition, Lifestyle, Healthspan. (Min.5-Max. 8)

Available analytical panels, Health Bio Care Genetik + Epigenetik

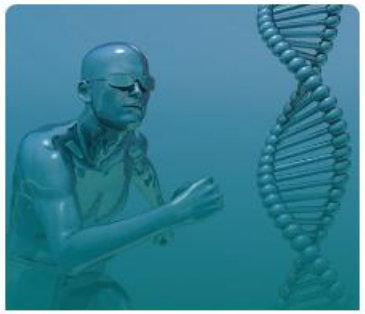
GENEOMETRY® METABOLIC HEALTH PANEL

Personalized nutrition with accompanying control of epigenetic markers

Do you want to lose weight or simply eat healthier?

Details

Evaluation



GENEOMETRY® HEALTHY SPORT PANEL

Molecular fitness tracking & tailored training and nutrition recommendations

Improve your athletic performance, whether you have been training for a long time or are just starting out.

Details

GENEOMETRY® HEALTHY AGING

Individualized prevention for your sensitive aging mechanisms

Find out your biological age and how you can properly support your body during “inflammaging.”

Details

GENEOMETRY® STRESS MONITOR PANEL

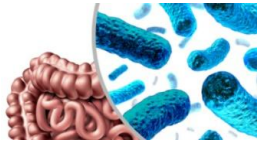
Epigenetic analysis of stress regulation

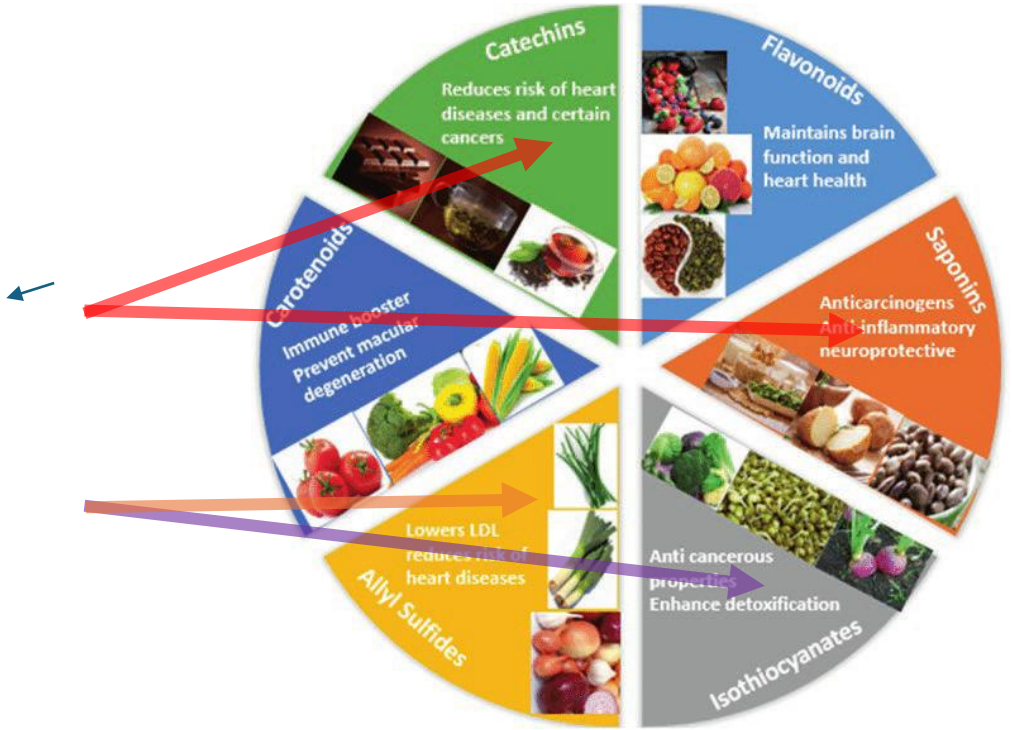
Prevent chronic stress or stress-related illnesses early on.

Details

Evaluation example

Personalisierung von Zusatzstoffen zur Krankheitsprävention nach Analyse der grundlegenden Merkmale von Gesundheit und Alterung. Das Blue Zones-Konzept: personalisierte Zusatzstoffe





REVIEW

Epigenetic mechanisms in anti-cancer actions of bioactive food components – the implications in cancer prevention

Review Article

FFHD

Functional Foods in Health and Disease

Mechanisms of selected functional foods against viral infections with a view on COVID-19: Mini review

REVIEW

Therapeutic perspectives of epigenetically active nutrients

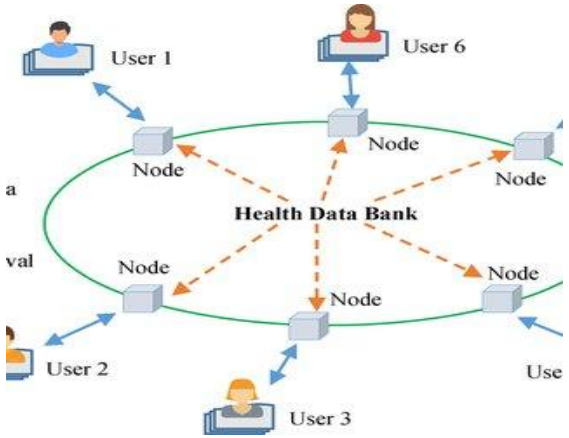
Research Article

EGCG Prevents High Fat Diet-Induced Changes in Gut Microbiota, Decreases of DNA Strand Breaks, and Changes in Expression and DNA Methylation of *Dnmt1* and *MLH1* in C57BL/6J Male Mice

ORIGINAL CONTRIBUTION

Gallic acid, a common dietary phenolic protects against high fat diet induced DNA damage

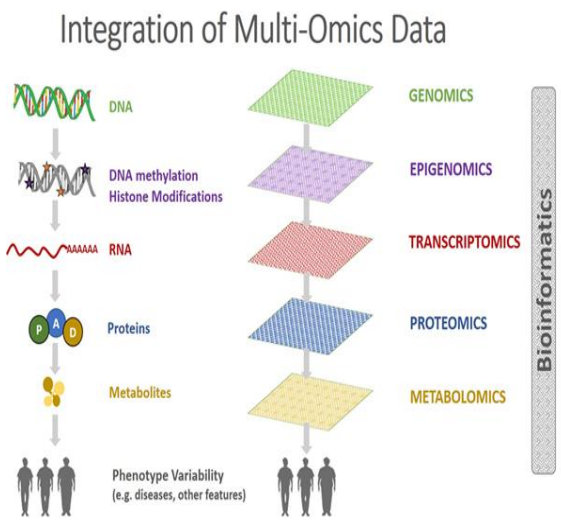
Quo vadis: Daten aus klinischen, Ernährungsanalysen, Fragebögen, persönlichen Trackern werden erfasst und in Gesundheitsdatenbanken analysiert und verglichen

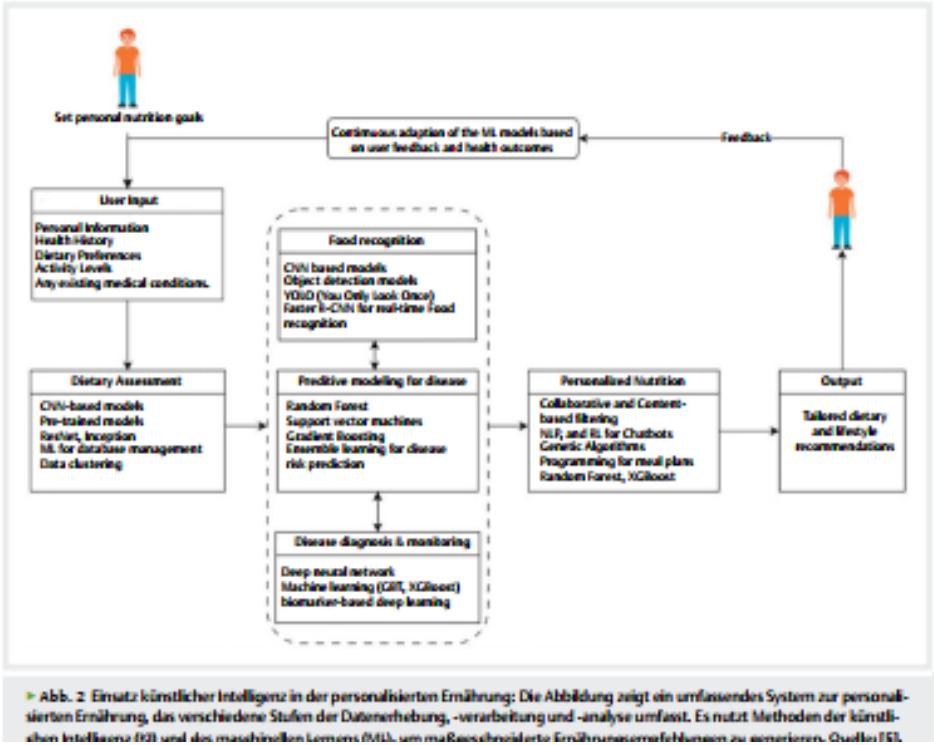


- **Compared with controls**
- **Analysed with KI, decision tree**

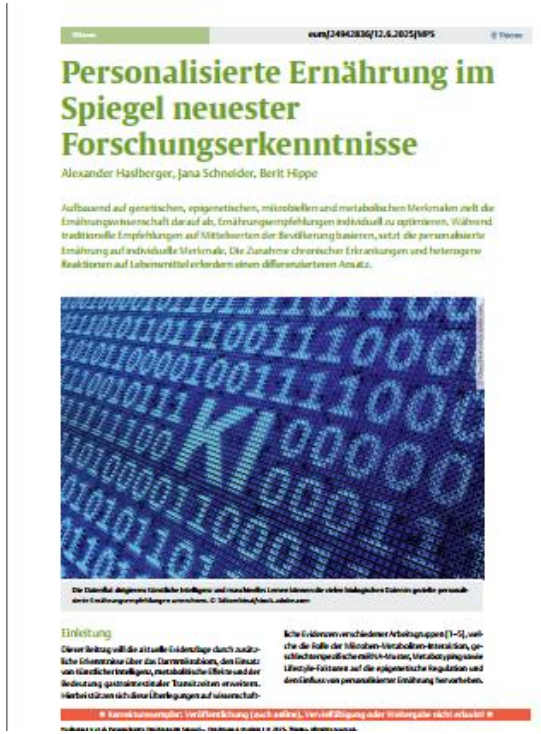
- **Guidance**
- **Prevention**
- **Intervention**

Integration von Daten aus verschiedenen OMICs notwendig, Bioinformatik, selbstlernende Algorithmen zur Auswertung, Prognose





▸ Abb. 2 Einsatz künstlicher Intelligenz in der personalisierten Ernährung: Die Abbildung zeigt ein umfassendes System zur personalisierten Ernährung, das verschiedene Stufen der Datenerhebung, -verarbeitung und -analyse umfasst. Es nutzt Methoden der künstlichen Intelligenz (KI) und des maschinellen Lernens (ML), um maßgeschneiderte Ernährungsempfehlungen zu generieren. Quelle: [53]



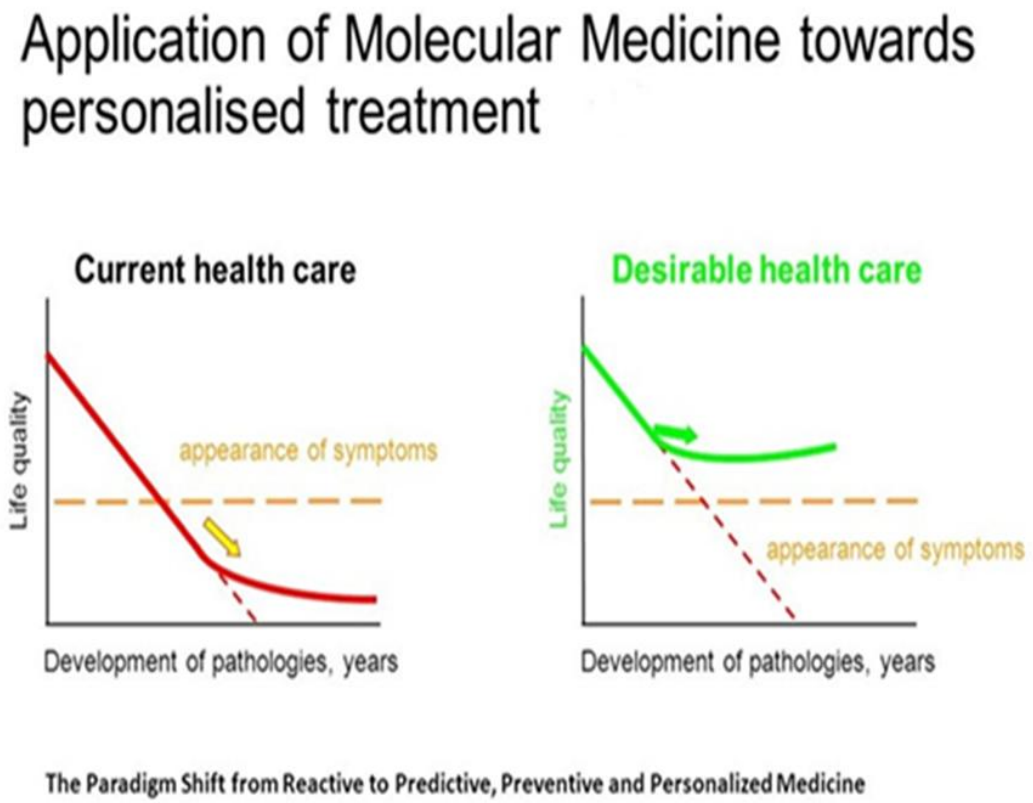
Personalisierte Ernährung im Spiegel neuester Forschungserkenntnisse

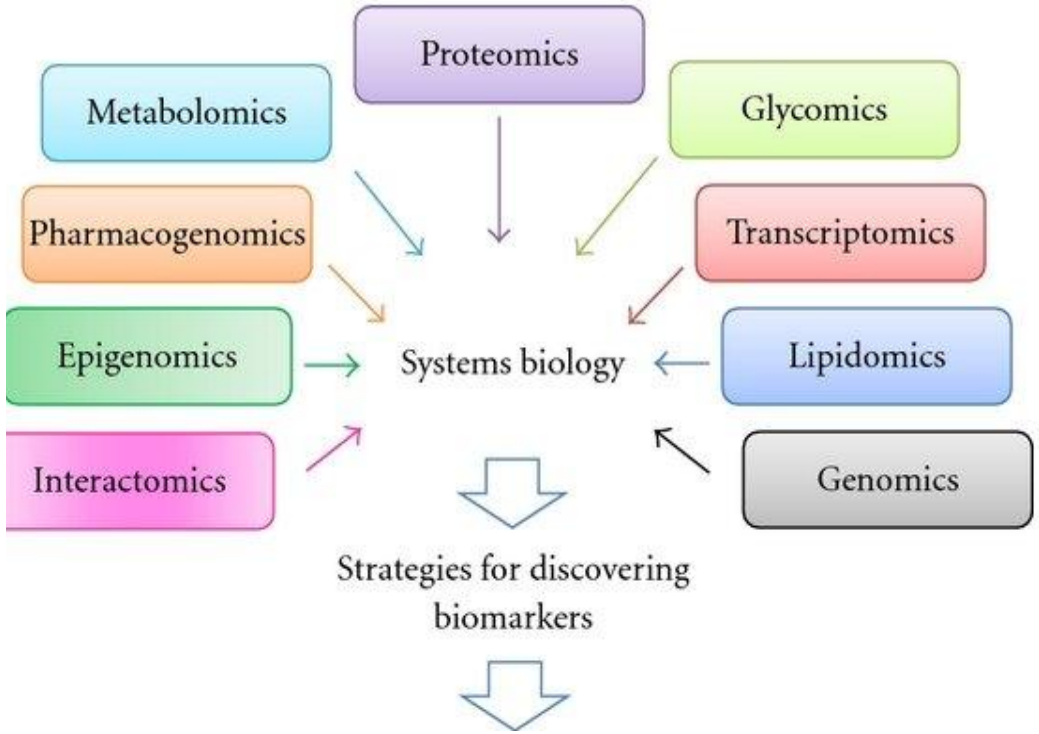
Alexander Haslberger, Jana Schneider, Berit Hippe

Aufbauend auf genetischen, epigenetischen, mikrobiellen und metabolischen Merkmalen zielt die Ernährungswissenschaft darauf ab, Ernährungsempfehlungen individuell zu optimieren. Während traditionelle Empfehlungen auf Mittelwerten der Bevölkerung basieren, setzt die personalisierte Ernährung auf individuelle Merkmale. Die Zunahme chronischer Erkrankungen und heterogene Reaktionen auf Lebensmittel erfordern einen differenzierteren Ansatz.

Einleitung

Prävention, Personalisierung: von einem OMICS marker- basierter Systemischen Gesundheitsverständnis zu salutogenen Gesundheit (der Lehre vom Gesund-bleiben)

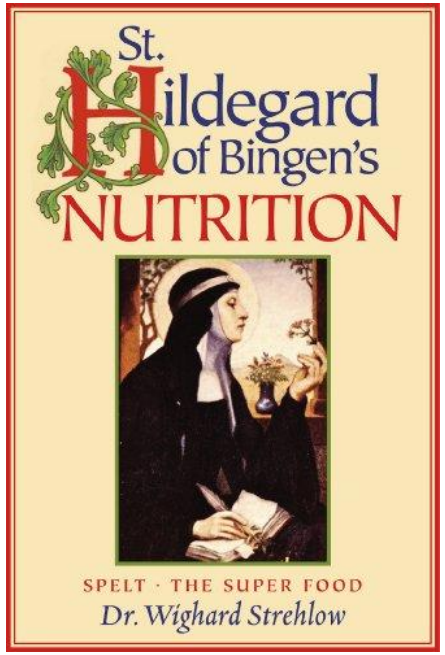




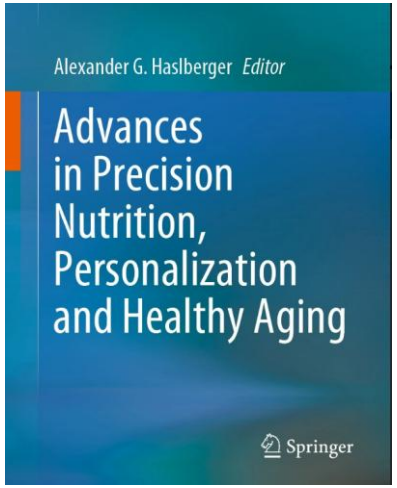
AH, 224

Paradigmen I: Aufgaben der Ernährung

Nutrition is the biochemical and physiological process by which an organism uses food to support its life.	Hippocrates, **“Let food be thy medicine, and let medicine be thy food”**



Paradigmen II: Pyramide : Personalisierung



Zwei scheinbar gegensätzliche Ansätze – der eine aus der Perspektive der globalen öffentlichen Gesundheit und der andere aus dem Paradigma einer präzisen personalisierten Ernährung – sollten harmonisiert und erörtert werden, da sie sich gegenseitig ergänzen und personalisierte, partizipative, präventive und prädiktive Strategien erforderlich sind, um einen Gesundheitszustand aufrechtzuerhalten und Krankheiten vorzubeugen und zu bewältigen.

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