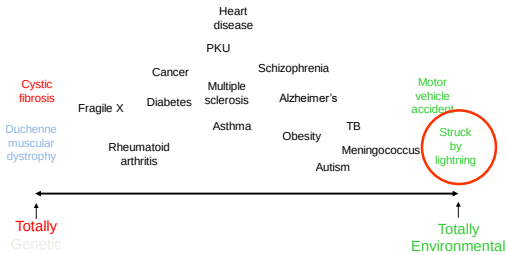
Ernährung als Wissenschaft, 2017
Forschungsgebiete: Novel food, Mikrobiota in Lebensmittel und Darm, Epigenetik;
Alexander G Haslberger

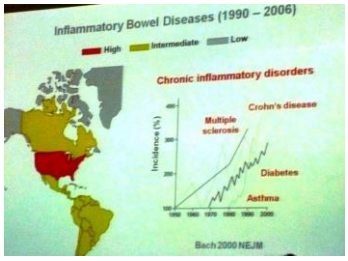
www.alexander-haslberger.at
https://www.researchgate.net/profile/Alexander_Haslberger

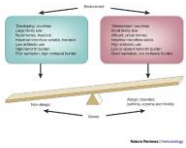
Dep. For Nutritional Sciences
universität wien

Phenotyp, Krankheiten: Genetik-Umwelt ?

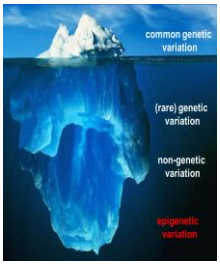


Anstieg komplexer Erkrankungen
Was verändert sich in der Umwelt ?



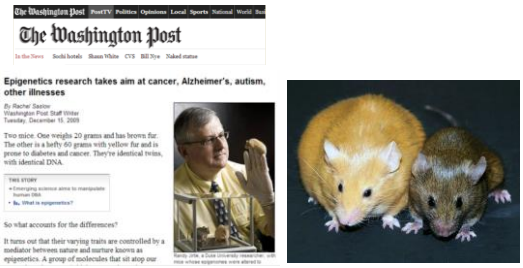


Missing heritability?
Genetik erklärt nur "wenig", Gen-Umwelt Interaktionen wichtiger ? Epigenetik



4

Break trough Epigenetik: Agouti mice: genetisch ident epigenetisch unterschiedlich. Einfluss Ernährung. Transgenerationale Effekte



The Washington Post

Epigenetics research takes aim at cancer, Alzheimer's, autism, other illnesses

By Rachel Saslow
Washington Post Staff Writer
Tuesday, December 15, 2009

Two mice. One weighs 20 grams and has brown fur. The other is a hefty 60 grams with yellow fur and is prone to diabetes and cancer. They're identical twins, with identical DNA.

THIS STORY
- Emerging science aims to manipulate human DNA
- So, What is epigenetics?

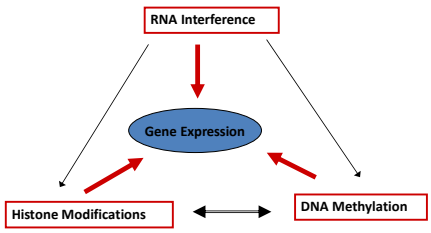
So what accounts for the differences?

It turns out that their varying traits are controlled by a mediator between nature and nurture known as epigenetics. A group of molecules that sit atop our

Epigenetics

- Epigenetics refers to the study of changes in the regulation of gene activity and expression that are not dependent on gene DNA sequence.
- While epigenetics often refers to the study of single genes or sets of genes, **epigenomics** refers to more global analyses of epigenetic changes across the entire **genome.**

Epigenetic Mechanisms



The environment, toxins influence epigenetic maschinery

Lynne Peeples
lynne.peeples@huffingtonpost.com

Toxic Environmental Exposures Could Cause Reproductive Harm Across Generations, Study Suggests

Posted: 05/03/2012 5:06 pm EDT | Updated: 05/03/2012 5:31 pm EDT

Int. J. Mol. Sci. **2012**, *13*, 10143-10153; doi:10.3390/ijms130810143

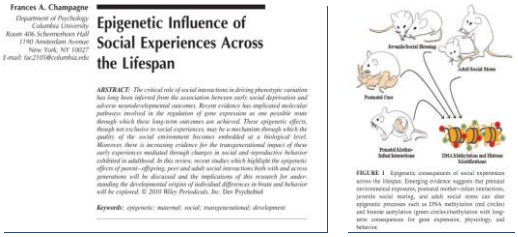
OPEN ACCESS
International Journal of
Molecular Sciences
ISSN 1422-0067
www.mdpi.com/journal/ijms

Review

Epigenetic Effects of Environmental Chemicals Bisphenol A and Phthalates

Sher Singh [1] and Steven Shoei-Lung Li [2,3,*]

The environment, stress, influences epigenetic control of gene expression



Frances A. Champagne
Department of Psychology, Columbia University, Room 406 Schermerhorn Hall, 1190 Amsterdam Avenue, New York, NY 10027
E-mail: fac2105@columbia.edu

Epigenetic Influence of Social Experiences Across the Lifespan

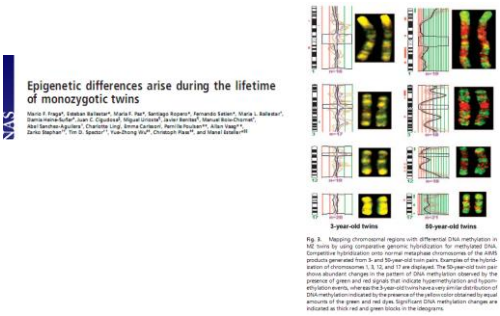
ABSTRACT: The critical role of social interactions in driving phenotypic variation has long been inferred from the association between early social deprivation and adverse neurodevelopmental outcomes. Recent evidence has implicated molecular pathways involved in the regulation of gene expression as one possible route through which these long-term outcomes are achieved. These epigenetic effects, though not exclusive to social experiences, may be a mechanism through which the quality of the social environment becomes embedded at a biological level. Moreover, there is increasing evidence for the transgenerational impact of these early experiences mediated through changes in social and reproductive behavior exhibited in adulthood. In this review, recent studies which highlight the epigenetic effects of parent–offspring, peer and adult social interactions both with and across generations will be discussed and the implications of this research for understanding the developmental origins of individual differences in brain and behavior will be explored. © 2010 Wiley Periodicals, Inc. Dev Psychobiol

Keywords: epigenetic; maternal; social; transgenerational; development

FIGURE 1 Epigenetic consequences of social experiences across the lifespan. Emerging evidence suggests that prenatal environmental exposures, postnatal mother–infant interactions, juvenile social mating, and adult social stress can alter epigenetic processes such as DNA methylation (red circles) and histone acetylation (green circles/methylation with long-term consequences for gene expression, physiology, and behavior.

Rev., Dev. Psychobiol. 2010

Epigenetik, Zwillingsstudien



NAS

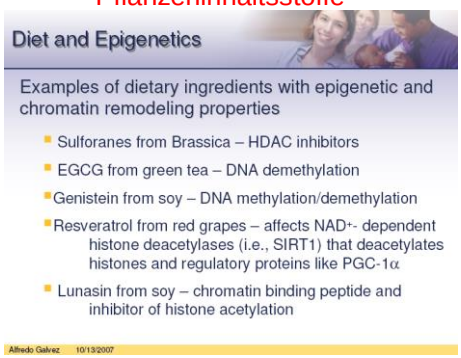
Epigenetic differences arise during the lifetime of monozygotic twins

Mario F. Fraga*, Esteban Ballestar*, María F. Paz*, Santiago Ropero*, Fernando Setien*, María L. Ballestar*, Damia Heine-Suñer*, Juan C. Cigudosa‡, Miguel Urioste§, Javier Benitez§, Manuel Boix-Chornet¶, Abel Sanchez-Aguilera¶, Charlotte Ling||, Emma Carlsson||, Pernille Poulsen**††, Allan Vaag**†, Zarko Stephan‡‡, Tim D. Spector‡‡, Yue-Zhong Wu§§, Christoph Plass§§, and Manel Esteller*¶¶

3-year-old twins 50-year-old twins

Fig. 3. Mapping chromosomal regions with differential DNA methylation in ME twins by using comparative genomic hybridization for methylated DNA. Competitive hybridization onto normal metaphase chromosomes of the MMS products generated from 3- and 50-year-old twin pairs. Examples of the hybridization of chromosomes 1, 5, 12, and 17 are displayed. The 50-year-old twin pair shows abundant changes in the pattern of DNA methylation observed by the presence of green and red signals that indicate hypermethylation and hypomethylation events, whereas the 3-year-old twins have a very similar distribution of DNA methylation indicated by the presence of the yellow color obtained by equal amounts of the green and red dyes. Significant DNA methylation changes are indicated as thick red and green blocks in the ideograms.

Epigenetik: Intervention Pflanzeninhaltsstoffe



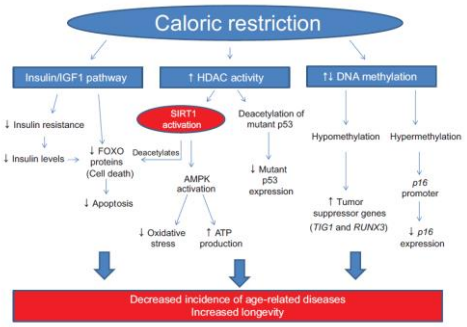
Diet and Epigenetics

Examples of dietary ingredients with epigenetic and chromatin remodeling properties

- Sulforanes from Brassica – HDAC inhibitors
- EGCG from green tea – DNA demethylation
- Genistein from soy – DNA methylation/demethylation
- Resveratrol from red grapes – affects NAD^+- dependent histone deacetylases (i.e., SIRT1) that deacetylates histones and regulatory proteins like PGC-1α
- Lunasin from soy – chromatin binding peptide and inhibitor of histone acetylation

Alfredo Galvez 10/13/2007

Caloric Restriction und Sirt foods



Epigenetische aktive Ernährung: Telomere und epigenetische Alterungsmarker

Journal of Nutrition & Food Sciences

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

Abstract

Objective: In vitro and in vivo studies in rodents have demonstrated many health promoting properties of individual phytochemicals including antioxidative and chemopreventive effects. Recently combination of substances is claimed to enhance activity.

The objective of this study was to investigate health benefits of a daily consumption of a combination of a large variety of phytochemicals (TimeBlock®). To assess potential changes we analyzed specific biomarkers that are associated with aging, oxidative stress and DNA stability: Methylation of *LINE-1, c-Myc, IL-6, MLH1, DNMT1, ITGAL2B* and telomere length.

Epigenetic active diet effects DNA repair

Switzeny et al. Clinical Epigenetics 2012, 4:19
http://www.clinicalepigeneticsjournal.com/content/4/1/19

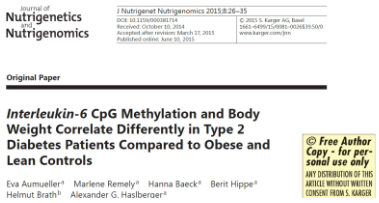
CLINICAL EPIGENETICS

RESEARCH Open Access

Vitamin and antioxidant rich diet increases *MLH1* promoter DNA methylation in DMT2 subjects

Olivier J Switzeny[1], Elisabeth Müllner[1], Karl-Heinz Wagner[1], Helmut Brath[2], Eva Aumüller[1] and Alexander G Haslberger[1*]

IL- 6 Genmethylierung und metabolisches Syndrom



Journal of Nutrigenetics and Nutrigenomics

J Nutrigenet Nutrigenomics 2015;8:26–35

Original Paper

***Interleukin-6* CpG Methylation and Body Weight Correlate Differently in Type 2 Diabetes Patients Compared to Obese and Lean Controls**

Eva Aumueller[a] Marlene Remely[a] Hanna Baeck[a] Berit Hippe[a] Helmut Brath[b] Alexander G. Haslberger[a]

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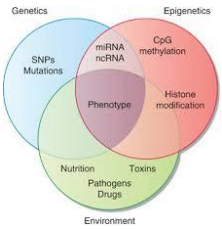
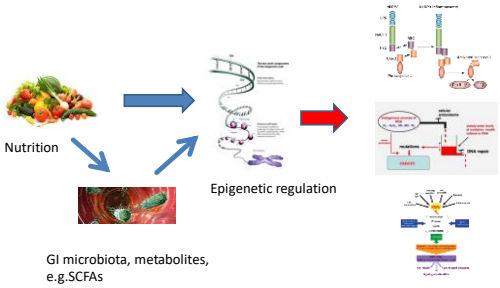
Ernährungsberatung: Moleculare Analysen für personalisierte Ernährung Genetik + Epigenetik (+ Mikrobiota)



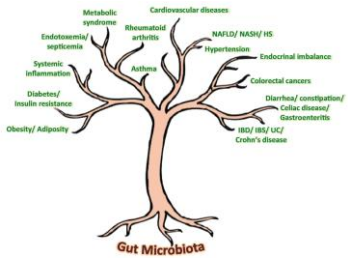
- Biological age
- Healthy aging
- DNA health, instability
- Metabolism and nutrition
- GI microbiota and brain axis
- Skin and beauty

Epigenetic active food components

Discussion, hypothesis: diets effect epigenetic regulation of inflammation, DNA damage, ageing (also) via GI-microbiota- metabolites ?

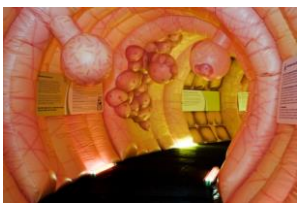


Most complex diseases, microbiota involved?



If you „google" microbiota + any complex disease and you find no science results for a specific disease: please tell me

Gesundheit: Rolle der (GI)- Microbiota, our commensals in the gut

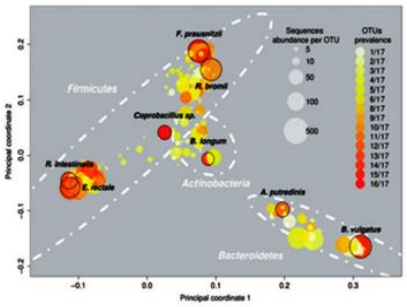


- Microbiome
- 10 -100x more information than the human genome

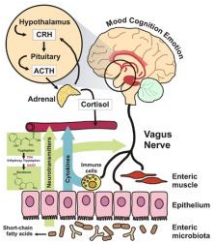
20

From plating of living bacteria to analysis of (r)DNA of bacteria

Major groups of the human microbiome



Elements of the gut brain axis: bacterial metabolites: from the gut through the blood into the brain ?



MICROBIAL ECOLOGY in Health and Disease

GUT IN FOCUS: EXTENDED ABSTRACT

Enteric short-chain fatty acids: microbial messengers of metabolism, mitochondria, and mind: implications in autism spectrum disorders

Derrick F. MacFabe*

The Kilee Patchett-Evans Autism Research Group, Departments of Psychology (Neuroscience) and Psychiatry, Division of Developmental Disabilities, University of Western Ontario, Ontario, Canada

GI microbiota: (Gene) diversity: highly desired

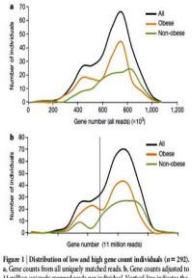
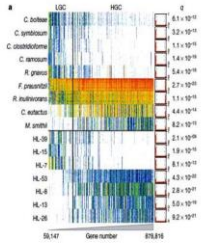


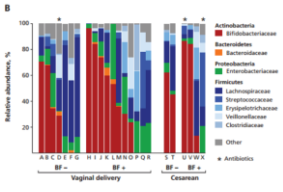
Figure 1 | Distribution of low and high gene count individuals (n = 292). a, Gene counts from all uniquely matched reads. b, Gene counts adjusted to 1 million uniquely mapped reads per individual. Vertical line indicates the threshold of the LGC and the HGS individuals; the observed bimodal distribution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



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

Ways of delivery and microbiota: a long lasting difference

Infants born by elective cesarean delivery had particularly low bacterial richness and diversity. formula-fed infants had increased richness of species, with overrepresentation of *Clostridium difficile*.




Gut microbiota of healthy Canadian infants: profiles by mode of delivery and infant diet at 4 months

CHILD involves more than 10 000 people, including 3 500 infants

Microbiota change in life time


Beratung

Mikrobiota im Laufe des Lebens:
Veränderung und Einflüsse auf die Darmbesiedlung

Für eine längerfristige Verbesserung oder Bewahrung der Mikrobiota-Balance werden künftig pro-, prebiotische Konzepte weiterhin wichtig sein. Allerdings könnte erst die Entwicklung von Probiotika mit Gruppen anaerober Spezies, wie z. B. Akkermansia oder F. prausnitzii zu signifikanten Erfolgen bei vielen Erkrankungen führen.

Geburt und Entwicklung der Mikrobiota

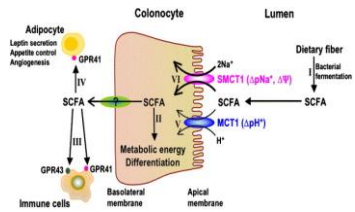
Diversität, Darmwand und Übergewicht

Microbiota and fermentation products e.g. SCFAs

Clostridial cluster IV (*Rumminococcaceae*)	*Clostridial cluster XIVa* (*Lachnospiraceae*)
Faecalibacterium prausnitzii *Butyricoccus* *Clostridium Leptum*	*Eubacterium hallii* *Anaerostipes coli* *Roseburia spp.* *E. rectale spp.*
Resistent starch	*Non starch Polysaccharides*

(Louis and Flint, 2009, FEMS)

SCFAs bind to G-Protein-Receptors 41/43 (FFARs) on Immune cells, Adipocytes,…

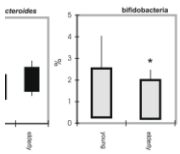


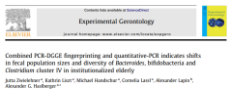
Anti-inflammatory;

Inhibition of NFκB

(Huster et al., 2013; Flint et al., 2009, Nature Rev)

Elderly: Decreased abundance, diversity and LAB



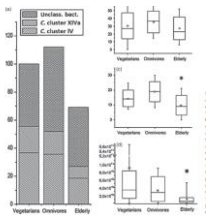


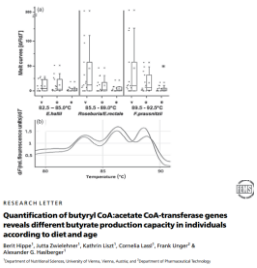
Experimental Gerontology

Combined PCR-DGGE fingerprinting and quantitative-PCR indicates shifts in fecal population sizes and diversity of Bacteroides, bifidobacteria and Clostridium cluster IV in institutionalized elderly

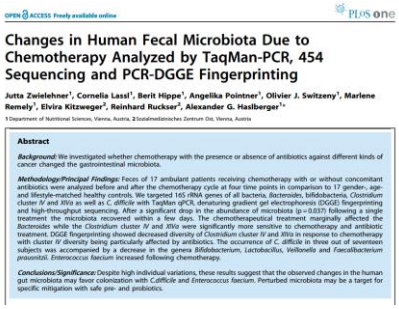
Jutta Zwielehner[a], Kathrin Lis[a], Michael Handschur[a], Cornelia Lassl[a], Alexander Lapin[a], Alexander G. Haslberger[a,*]

Decrease in SCFAs producers / „Butyrat Gen producing gene“ in elderly





Antobiotics and chemotherapy damage microbiota



OPEN ACCESS Freely available online

PLoS one

Changes in Human Fecal Microbiota Due to Chemotherapy Analyzed by TaqMan-PCR, 454 Sequencing and PCR-DGGE Fingerprinting

Jutta Zwielehner[1], Cornelia Lassl[1], Berit Hippe[1], Angelika Pointner[1], Olivier J. Switzeny[1], Marlene Remely[1], Elvira Kitzweger[2], Reinhard Ruckser[2], Alexander G. Haslberger[1]*

1 Department of Nutritional Sciences, Vienna, Austria, 2 Sozialmedizinisches Zentrum Ost, Vienna, Austria

Abstract

Background: We investigated whether chemotherapy with the presence or absence of antibiotics against different kinds of cancer changed the gastrointestinal microbiota.

Methodology/Principal Findings: Feces of 17 ambulant patients receiving chemotherapy with or without concomitant antibiotics were analyzed before and after the chemotherapy cycle at four time points in comparison to 17 gender-, age- and lifestyle-matched healthy controls. We targeted 16S rRNA genes of all bacteria, Bacteroides, bifidobacteria, Clostridium cluster IV and XIVa as well as *C. difficile* with TaqMan qPCR, denaturing gradient gel electrophoresis (DGGE) fingerprinting and high-throughput sequencing. After a significant drop in the abundance of microbiota ($p = 0.037$) following a single treatment the microbiota recovered within a few days. The chemotherapeutical treatment marginally affected the *Bacteroides* while the *Clostridium* cluster *IV* and *XIVa* were significantly more sensitive to chemotherapy and antibiotic treatment. DGGE fingerprinting showed decreased diversity of *Clostridium* cluster *IV* and *XIVa* in response to chemotherapy with cluster *IV* diversity being particularly affected by antibiotics. The occurrence of *C. difficile* in three out of seventeen subjects was accompanied by a decrease in the genera *Bifidobacterium*, *Lactobacillus*, *Veillonella* and *Faecalibacterium prausnitzii*. *Enterococcus faecium* increased following chemotherapy.

Conclusions/Significance: Despite high individual variations, these results suggest that the observed changes in the human gut microbiota may favor colonization with *C.difficile* and *Enterococcus faecium*. Perturbed microbiota may be a target for specific mitigation with safe pre- and probiotics.

Probiotics/ Yakult protect against diarrhea

Food and Agricultural Immunology
2012, 1–16, iFirst article

Taylor & Francis

Effects of antibiotic therapy on the gastrointestinal microbiota and the influence of *Lactobacillus casei*

Angelika Pirker[a], Alexander Stockenhuber[b], Marlene Remely[a], Anna Harrant[a], Berit Hippe[a], Christoph Kamhuber[b], Krista Adelmann[b], Felix Stockenhuber[b] and Alexander G. Haslberger[a]*

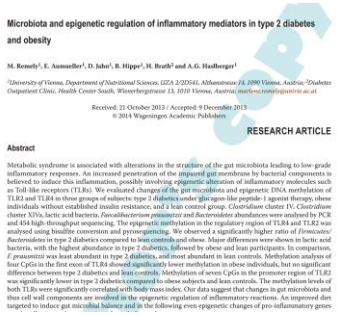
[a]*Department for Nutritional Sciences, University of Vienna, Vienna, Austria;* [b]*Krankenhaus Oberpallendorf, Vienna, Austria*

(*Received 13 January 2012; final version received 25 April 2012*)

Aims of methods. Effects of intervention with *Lactobacillus casei* Shirota (LcS) on the incidence of antibiotic-associated diarrhoea (AAD), *Clostridium difficile* infection (CDI) and changes in faecal microbiota were analysed using *C. difficile* ELISA (678 patients), qPCR using 16S rRNA group-specific primers, *C. difficile*-toxin kit and polymerase chain reaction/denaturing gradient gel electrophoresis (56 patients).
Results. As much as 18.5% of antibiotic treated group developed AAD, but only 5% of patients treated with antibiotics and LcS. Following antibiotic therapy, a decrease in the abundance of total Bacteria, *Clostridium* cluster IV and XI, *Bifidobacterium* spp. and butyryl-CoA CoA transferase genes was observed, whereas Enterobacteriaceae increased. LcS intervention reduced the antibiotic-associated decrease in the diversity of microbiota, increased the abundance of *Lactobacillus* spp. and reduced the antibiotic-induced decrease of *Bifidobacterium* spp.
Conclusions. Antibiotic treatment affects the diversity and the composition of the microbiota impairing butyrate production. Intervention with certain *Lactobacillus* strains may antagonise some of these changes, and more potent short-chain fatty acid-stimulating probiotics are desirable for intervention in AAD.

Keywords: antibiotics; antibiotic-associated diarrhoea; bacterial; *Clostridium difficile* infection; gastrointestinal microbiota; *Lactobacillus casei*

Microbiota different in obesity



Microbiota and epigenetic regulation of inflammatory mediators in type 2 diabetes and obesity

M. Remely[1], E. Aumueller[1], D. Jahn[1], B. Hippe[2], H. Brath[2] and A.G. Haslberger[1]

[1]University of Vienna, Department of Nutritional Sciences, UZA 2/2D541, Althanstrasse 14, 1090 Vienna, Austria; [2]Diabetes Outpatient Clinic, Health Center South, Wienerbergstrasse 13, 1010 Vienna, Austria; marlene.remely@univie.ac.at

Received: 21 October 2013 / Accepted: 9 December 2013
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RESEARCH ARTICLE

Abstract

Metabolic syndrome is associated with alterations in the structure of the gut microbiota leading to low-grade inflammatory responses. An increased penetration of the impaired gut membrane by bacterial components is believed to induce this inflammation, possibly involving epigenetic alteration of inflammatory molecules such as Toll-like receptors (TLRs). We evaluated changes of the gut microbiota and epigenetic DNA methylation of TLR2 and TLR4 in three groups of subjects: type 2 diabetics under glucagon-like peptide-1 agonist therapy, obese individuals without established insulin resistance, and a lean control group. *Clostridium* cluster IV, *Clostridium* cluster XIVa, lactic acid bacteria, *Faecalibacterium prausnitzii* and *Bacteroides* abundances were analysed by PCR and 454 high-throughput sequencing. The epigenetic methylation in the regulatory region of TLR4 and TLR2 was analysed using bisulfite conversion and pyrosequencing. We observed a significantly higher ratio of *Firmicutes*/*Bacteroidetes* in type 2 diabetics compared to lean controls and obese. Major differences were shown in lactic acid bacteria, with the highest abundance in type 2 diabetics, followed by obese and lean participants. In comparison, *F. prausnitzii* was least abundant in type 2 diabetics, and most abundant in lean controls. Methylation analysis of four CpGs in the first exon of TLR4 showed significantly lower methylation in obese individuals, but no significant difference between type 2 diabetics and lean controls. Methylation of seven CpGs in the promoter region of TLR2 was significantly lower in type 2 diabetics compared to obese subjects and lean controls. The methylation levels of both TLRs were significantly correlated with body mass index. Our data suggest that changes in gut microbiota and thus cell wall components are involved in the epigenetic regulation of inflammatory reactions. An improved diet targeted to induce gut microbial balance and in the following even epigenetic changes of pro-inflammatory genes

in Diabetes produce microbiota less short chain fatty acids

Contents lists available at ScienceDirect

Gene

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

Effects of short chain fatty acid producing bacteria on epigenetic regulation of FFAR3 in type 2 diabetes and obesity

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Fasting is good for microbiota

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ERNÄHRUNG 20.11.2014

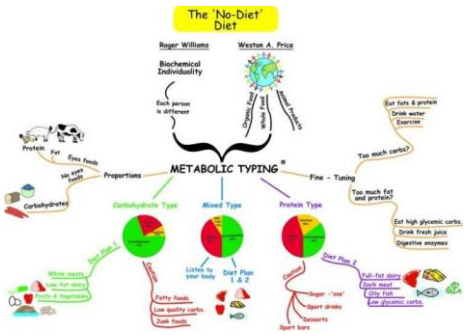
Fastenkuren sind gut für den Darm

Studien aus der Tierwelt haben schon öfters bewiesen, dass Fasten das Leben verlängern kann. Untersuchungen zu Menschen gibt es vergleichsweise wenig. Ein Wiener Forscher hat nun aber 60 Probanden im Dienste der Wissenschaft fasten lassen. Ergebnis: Neben allgemeinem Wohlbefinden konnte sich auch die Darmflora erholen.

Ernährungsgewohnheiten, Lebensstil, Medikamente und Lebensmittelzusatzstoffe führen oft zu Darmproblem und zur Beeinflussung der Mikrobiota, der Darmflora. Die Wissenschaftler des Instituts für Ernährungswissenschaft an der Universität Wien wussten im Vorfeld der Studie, dass eine gestörte Mikrobiota nur schwer zu beeinflussen ist. Man hatte Angst, dass durch das Fasten auch gute Darmbakterien zerstört werden können, erklärte Alexander Haslberger am Donnerstag bei einer Pressekonferenz in Wien.

Anstieg der bakteriellen Diversität

Metabotypes
The kind of metabolism that an individual has.



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