Mediterranean Diet, Functional Foods and Bioactive Compounds: Science and Practice

30th International Conference of FFC - 18th International Symposium of ASFFBC

September 23-25, 2022, Department of Food Science and Nutrition, University of the Aegean, Myrina, Lemnos, Greece

Fasting, CR and fasting- mimetics: Epigenetics, microbiota and personalisation

Haslberger G Alexander

University Vienna, Dep. f. Nutrition

Genetics, Microbiota and Epigenetics

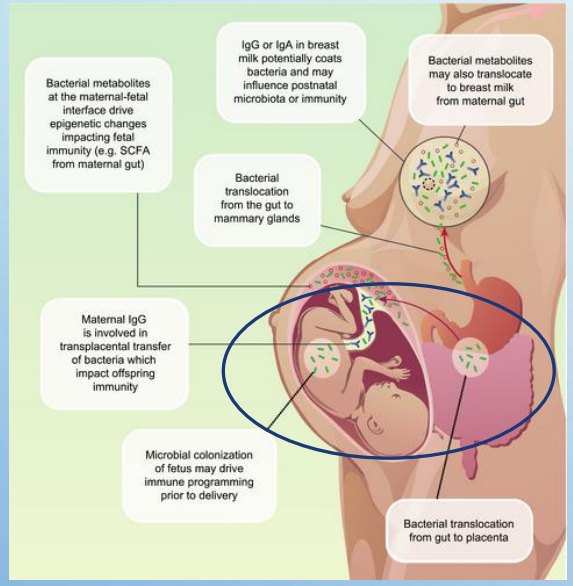
Fasting

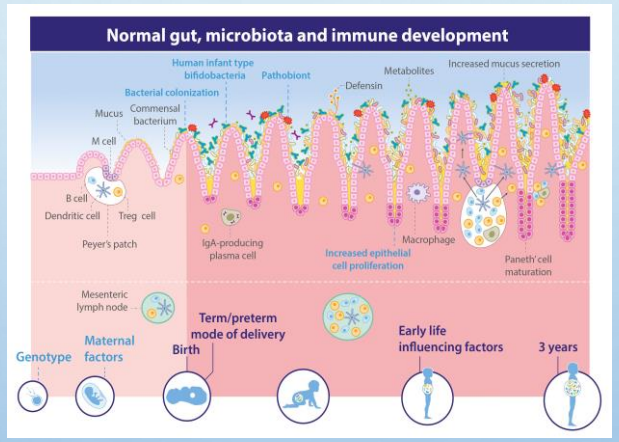
Fasting mimetics,

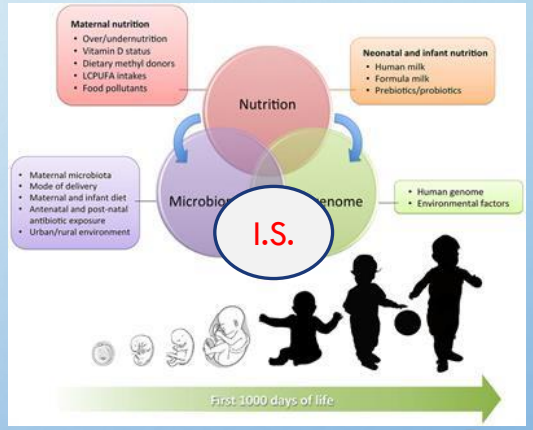
Personalisation

HealthBioCare GmbH

DEVELOPMENT OF MICROBIOTA, I.S., AND THE EPIGENETIC SYSTEM, FIRST1000 DAYS OF LIFE

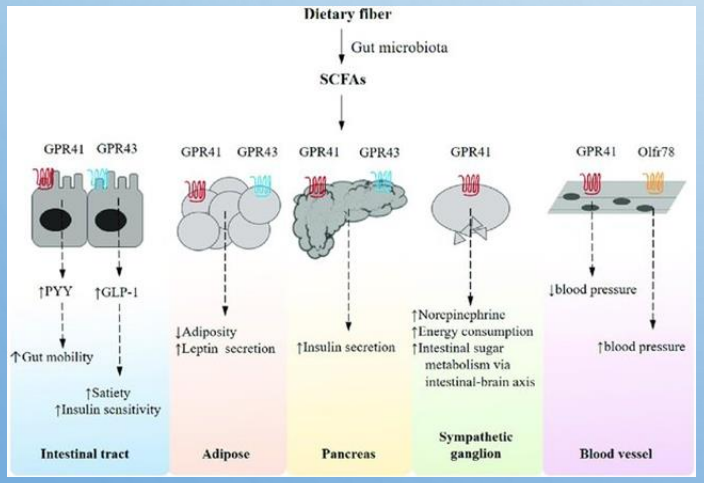


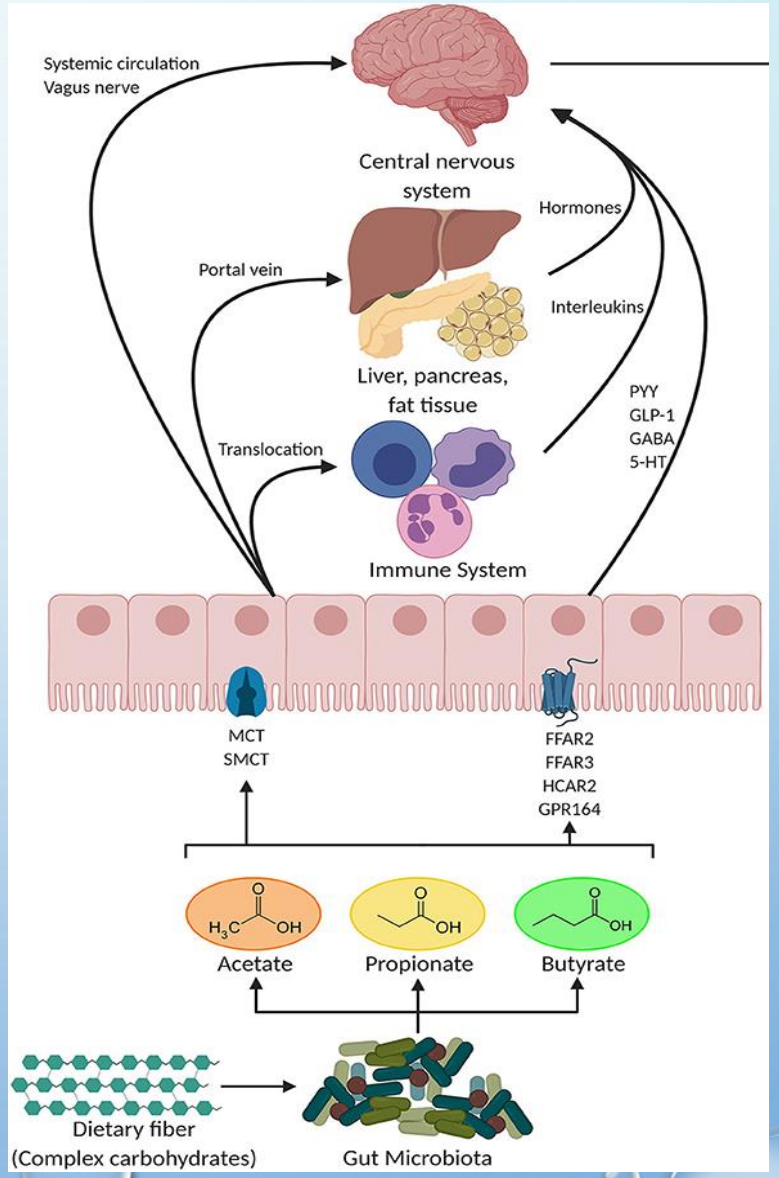




Development prenatal, Interaction with I.S., epigenetic maternal factors,
Diversity:delivery, breastfeeding, imprinting in 1000 days of life

DIET- GUT-MICROBIOTA I.S.,- CNS, EPIGENETIC AXIS



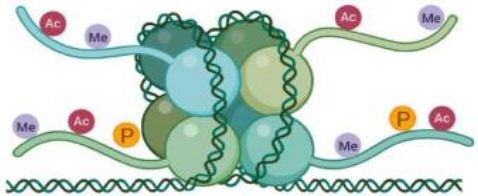


DIETARY INGREDIENTS AND MICROBIOTA-DERIVED METABOLITES (SCFAS) ADDRESS ALL ELEMENTS OF THE EPIGENETIC SYSTEM, ESP. SIRTUINS

DNA Methylation

DNA Methyl Transferase
- Capsaicin
- Curcumin
- Diallyl Sulphide
- Luteolin

Histone Modifications



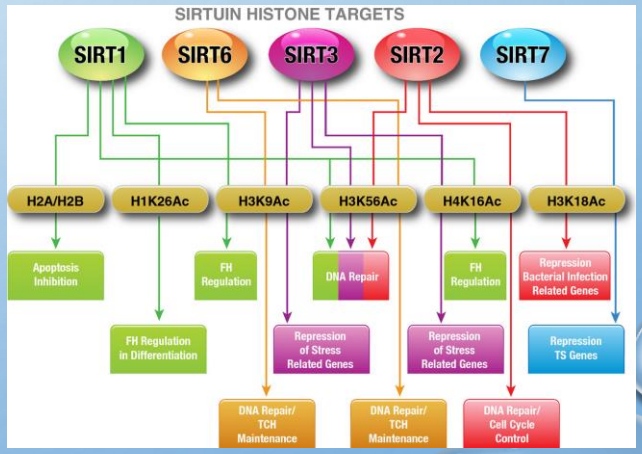
Histone Acetylation
- 6-Shogoal
- Anethole
- Capsaicin
- Curcumin
- Diallyl disulphide
- Diallyl trisulphide
- Garcinol
- Lapiferin
- Luteolin
- Sesamin
- α Mangostin
- γ Bisabolene

Histone Methylation
- Basil Polysaccharides
- Luteolin

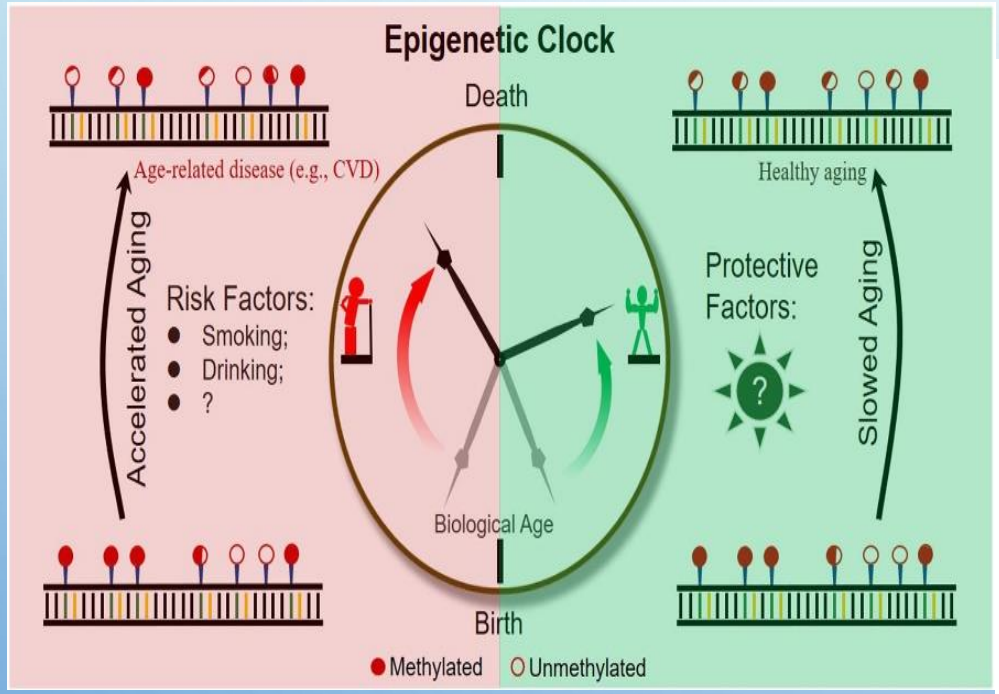
Histone Phosphorylation
- Luteolin

miRNA

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



AGING, DIETS, AND THE EPIGENETIC CLOCK, CPG- DNA METHYLATION;



AG Haslberger

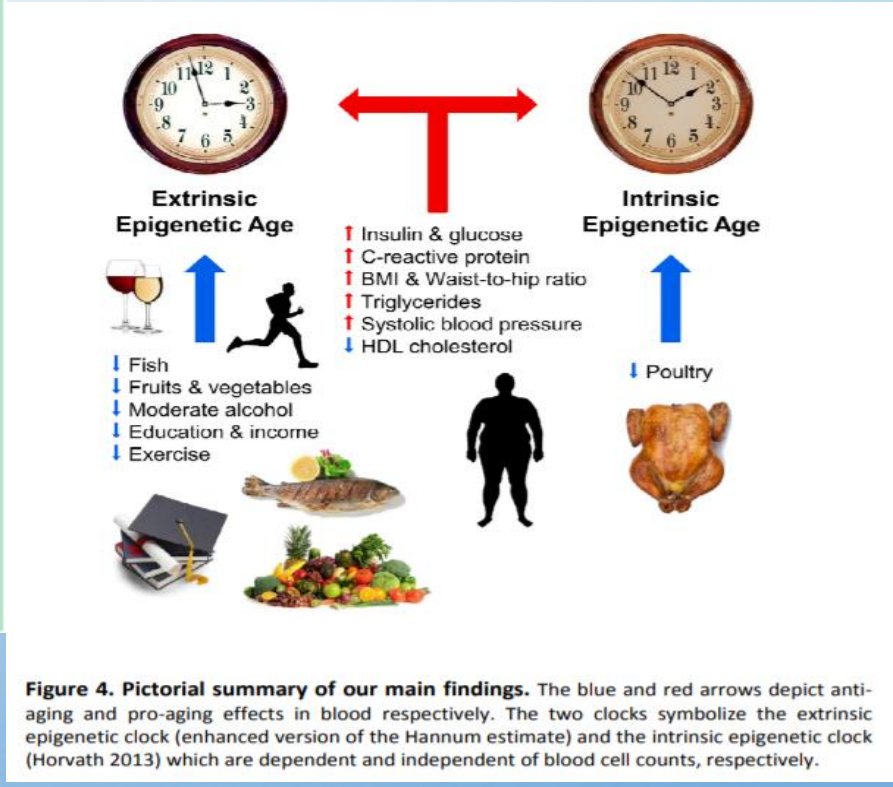
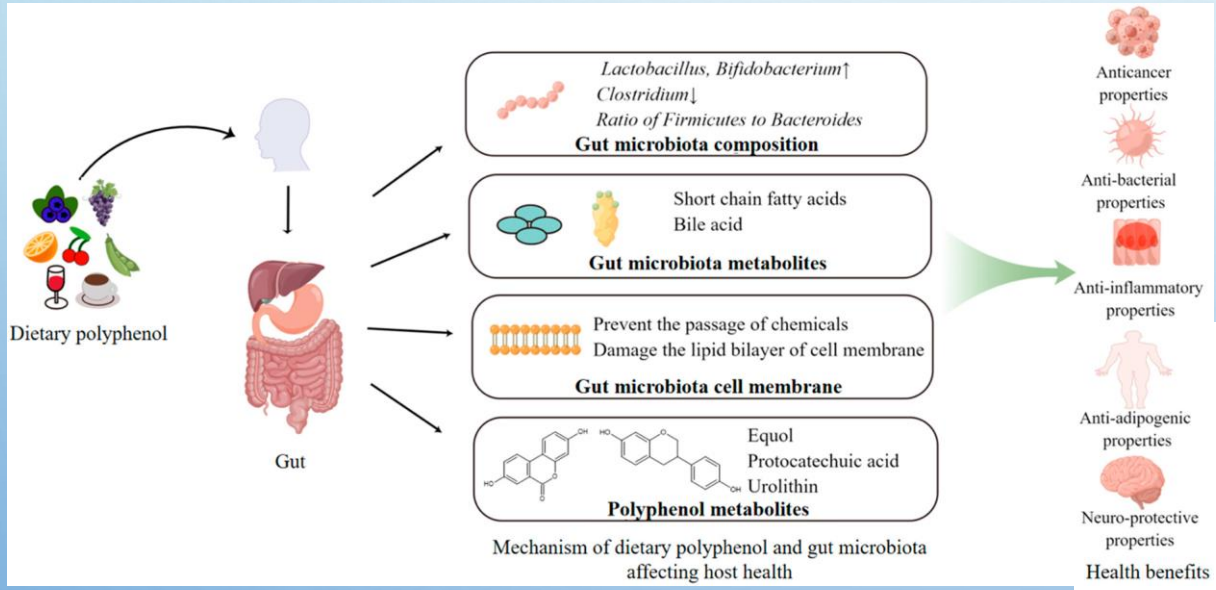
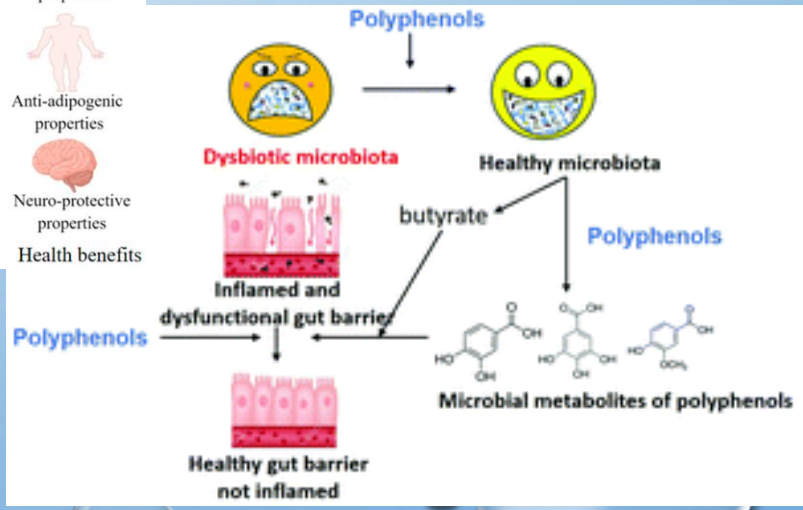


Figure 4. Pictorial summary of our main findings. The blue and red arrows depict anti-aging and pro-aging effects in blood respectively. The two clocks symbolize the extrinsic epigenetic clock (enhanced version of the Hannum estimate) and the intrinsic epigenetic clock (Horvath 2013) which are dependent and independent of blood cell counts, respectively.

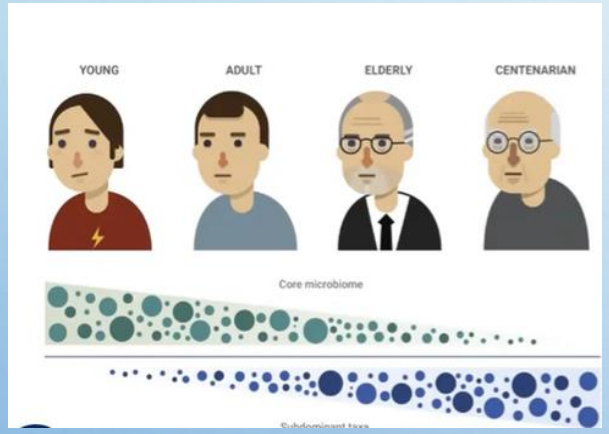
DIETS, POLYPHENOLS AND MICROBIOTA

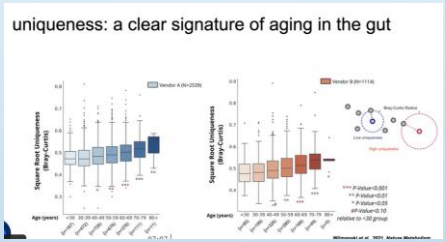


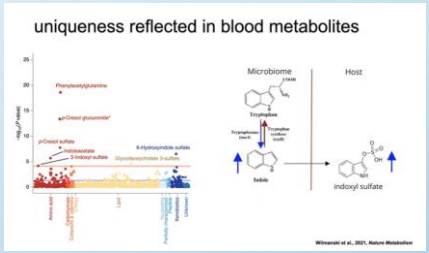
Mechanism of dietary polyphenol and gut microbiota affecting host health



AGING, BACTERIAL DIVERSITY AND HEALTH







Contents lists available at ScienceDirect

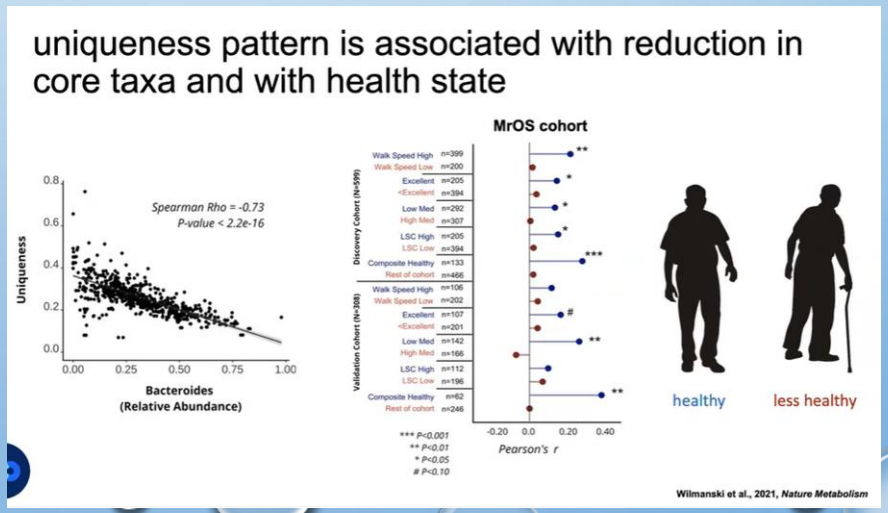
Experimental Gerontology

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

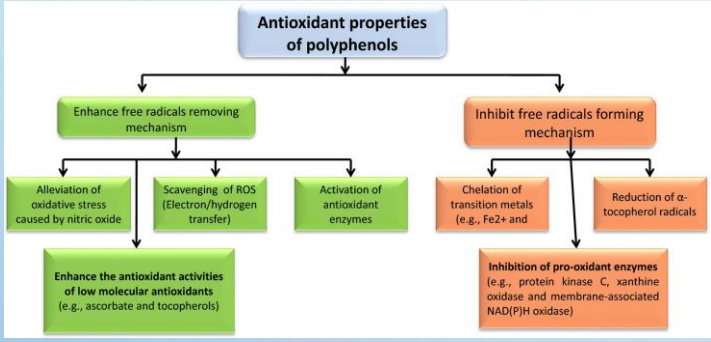
Combined PCR-DGGE fingerprinting and quantitative-PCR indicates shifts in fecal population sizes and diversity of *Bacteroides*, bifidobacteria and *Clostridium* cluster IV in institutionalized elderly

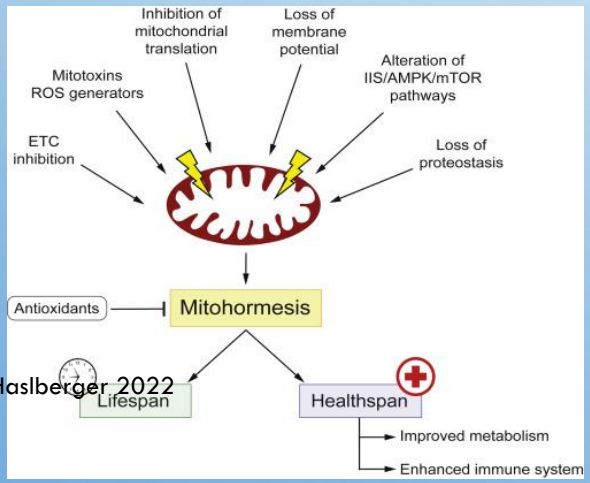
Jutta Zwielehner [a], Kathrin Liszt [a], Michael Handschur [a], Cornelia Lassl [a], Alexander Lapin [b], Alexander G. Haslberger [a,*]

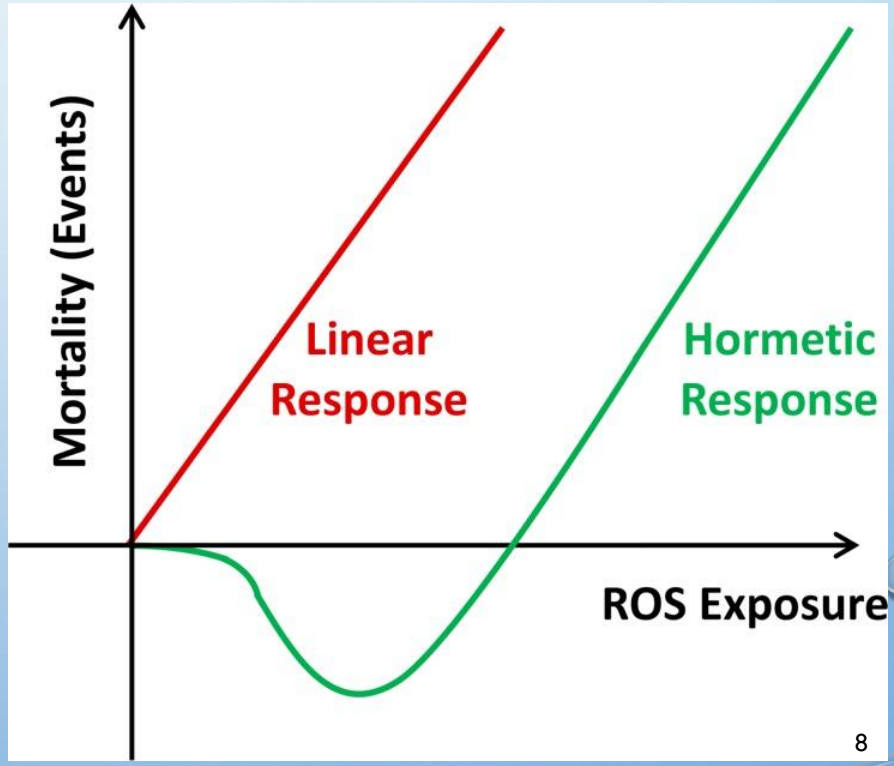
[a] Department of Nutritional Sciences, University of Vienna, Austria
[b] Sozialmedizinisches Zentrum Sophienspital, 1070 Wein, Apollogasse 19, Austria



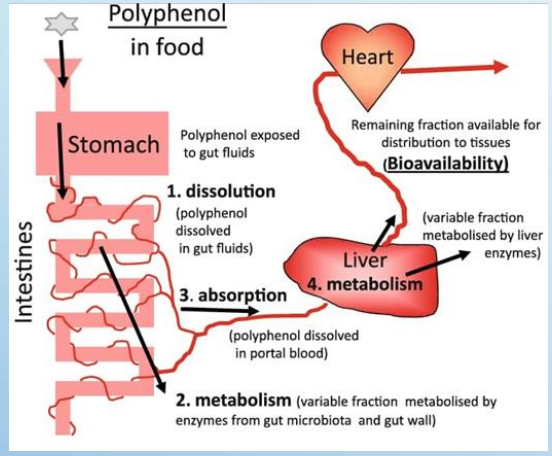
POLYPHENOLS: ANTI-OXYDATIVE, ROS BUT SOME ROS NEEDED MITOHORMESIS !

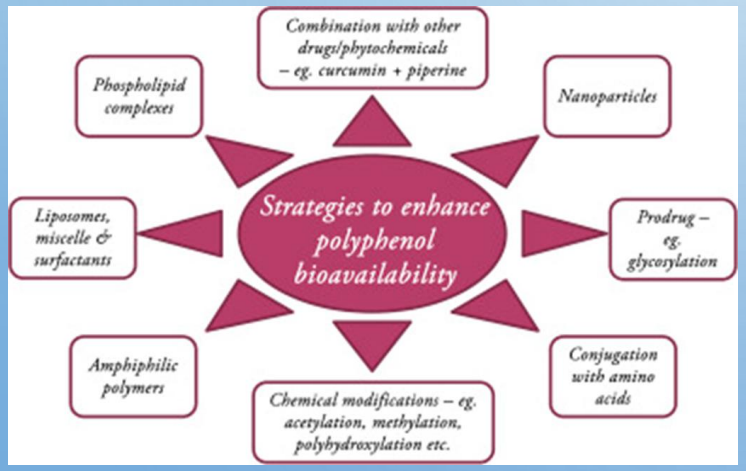






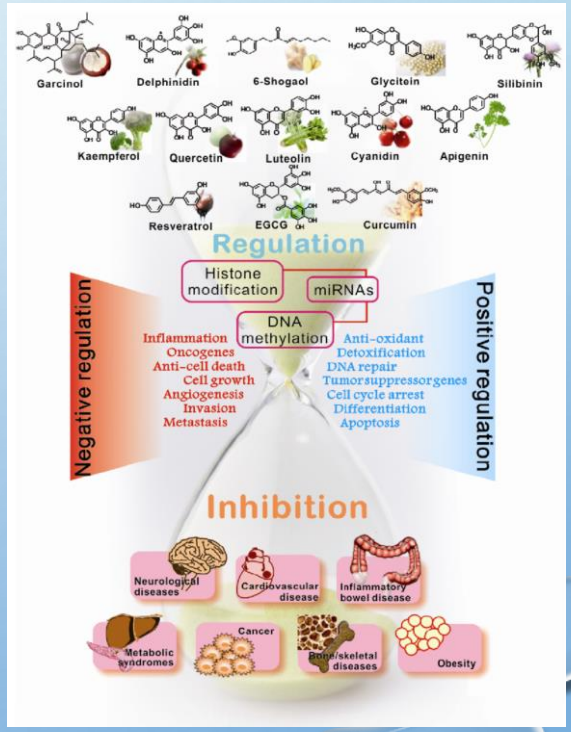
PLANT ADDITIVES : STABILTY, BIOACTIVITY ANTI-OXYDATIV : MICROBIOTA- EPIGENETICS



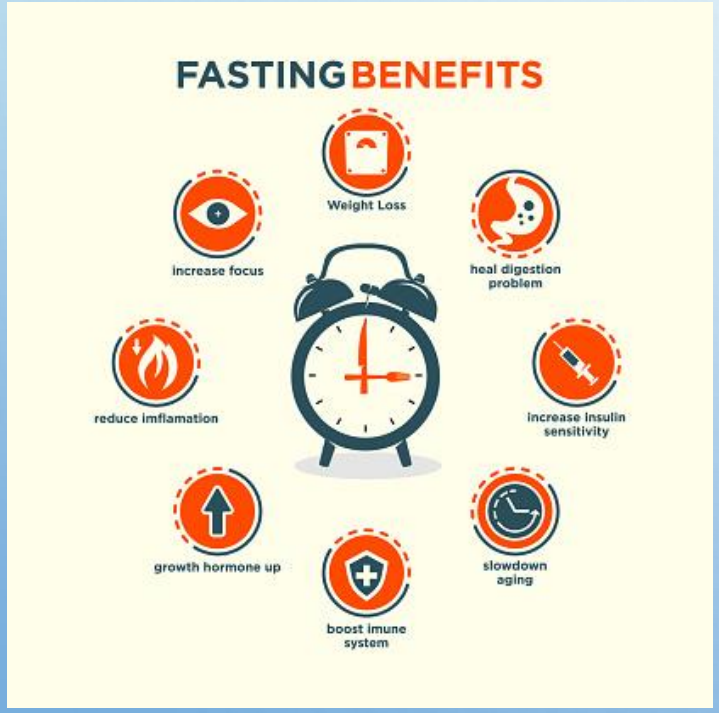


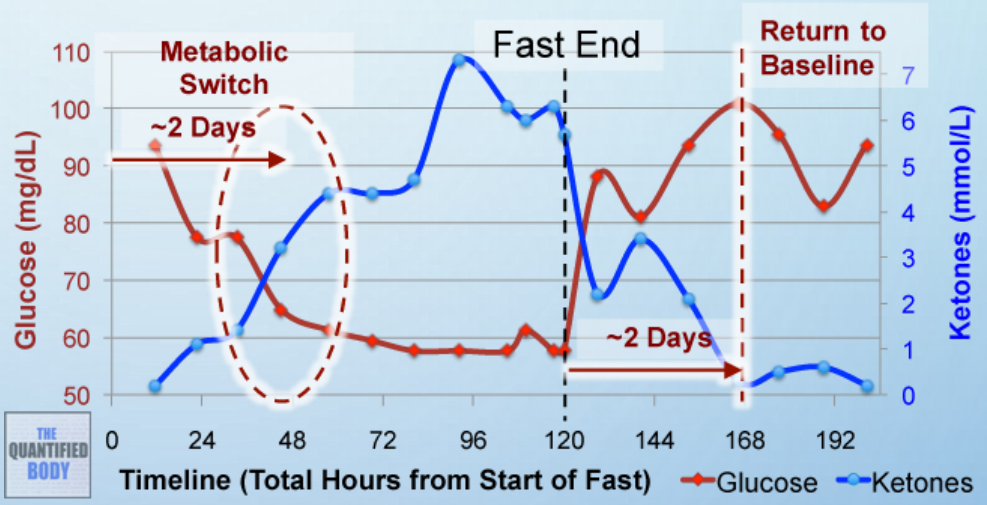
Enhancing:

Plant extracts
Nutraceuticals
Additives
Functional foods
Novel foods, EU
Dietary foods
Medicinal foods
Pharmaceutics
???



FASTING: EPIGENETIC HIGHLY ACTIVE BUTYRATE, BHB





SCIENTIFIC REPORTS

OPEN

Caloric restriction promotes functional changes involving short-chain fatty acid biosynthesis in the rat gut microbiota

C.R, FASTING: DIET IN MOUNT ATHOS MOUNTAIN TEA IS PART OF MEDITERANEAN DIET

Diet of the monks of Mount Athos

January 23, 2021

The monks lead a modest life from a food point of view, not to mention processed foods, meals are taken quietly, which is why the church faces on Mount Athos have a life expectancy ten years longer than the ordinary Greek. This lifestyle is the subject of a book that teaches you how to live, not just how to lose weight.

According to nutrition experts, the Mediterranean diet and fasting days, to the same extent, contribute to weight loss.

Orthodox monks on Mount Athos eat almost exclusively unprocessed, low-fat foods. In addition, on fasting days, monks drastically reduce their caloric intake, he writes Daily Mail.

Sideritis

cosmos philly

Greek-American News from Philadelphia

COMMUNITY CHURCHES ORGANIZATIONS SOCIETIES CA

SPORTS BLOGS

FOOD

Greek Mountain Tea as a part of the healthful Mediterranean diet

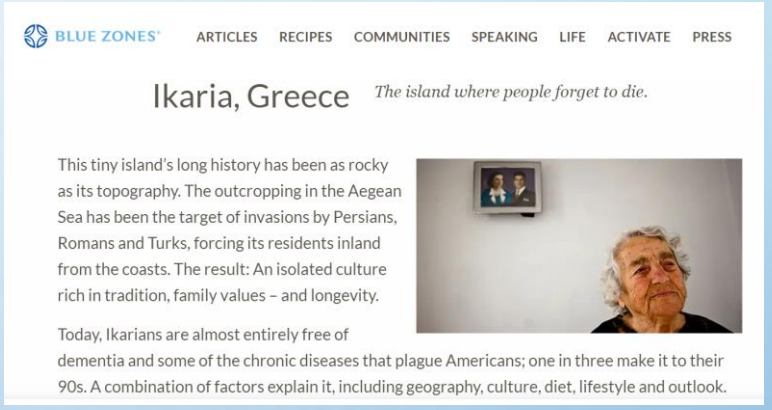
Posted by Cosmos Philly on May 24, 2015 Comment

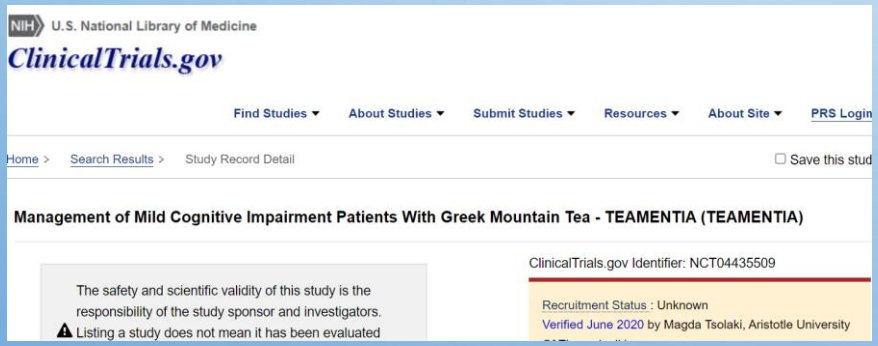
https://www.limnos-shop.gr › product · Translate this page

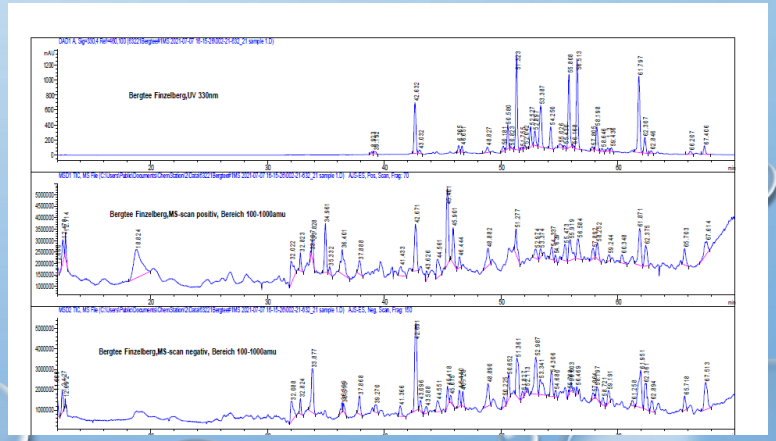
ΤΣΑΙ ΒΟΥΝΟΥ 10 TEABAGS - Limnos-shop.gr

Organic Greek **mountain tea** from **Lemnos**. Taste – Warm, lemony, mild and sweet taste. Constituents – Greek **mountain tea**. 10 servings per pouch ...

MOUNTAIN TEA IN BLUEZONE IKARIA ALZHEIMER,

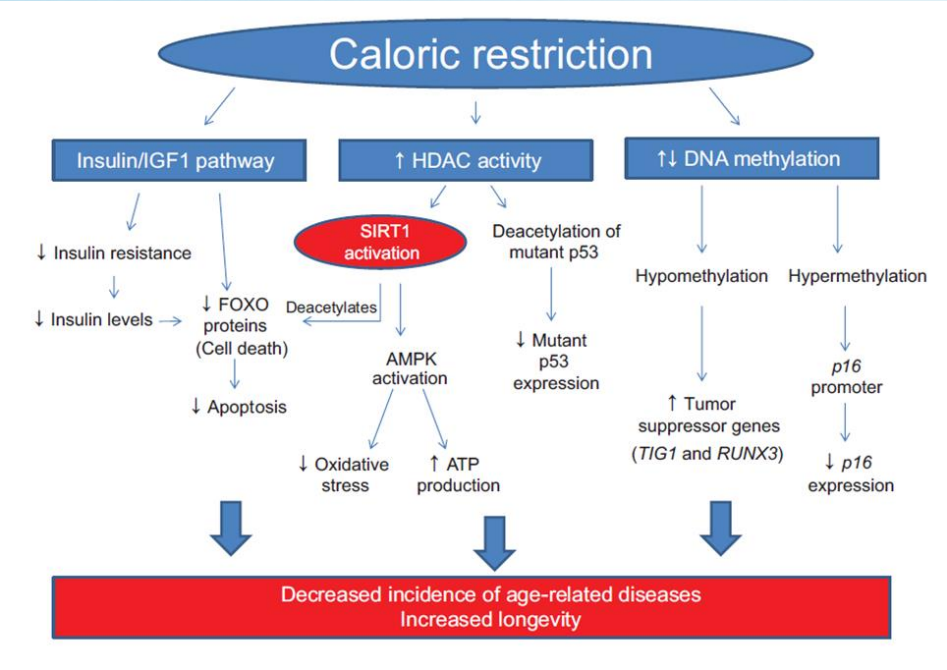


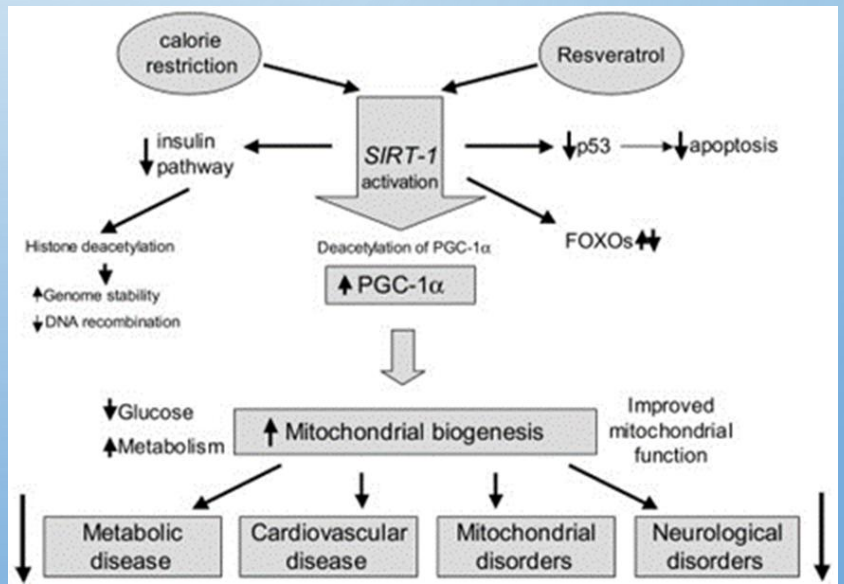




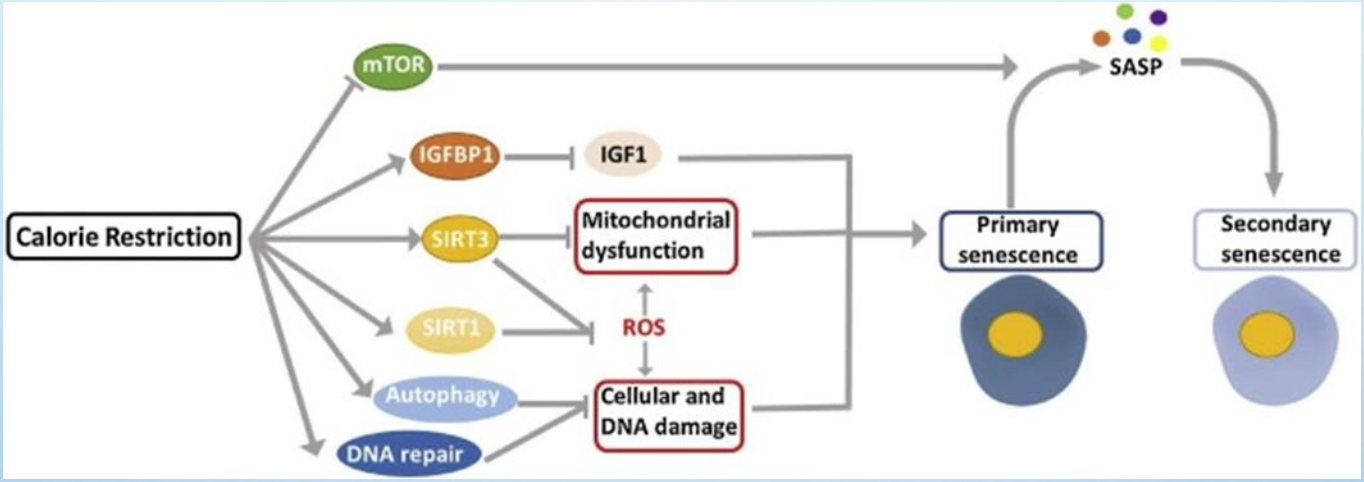
Ferulic acid

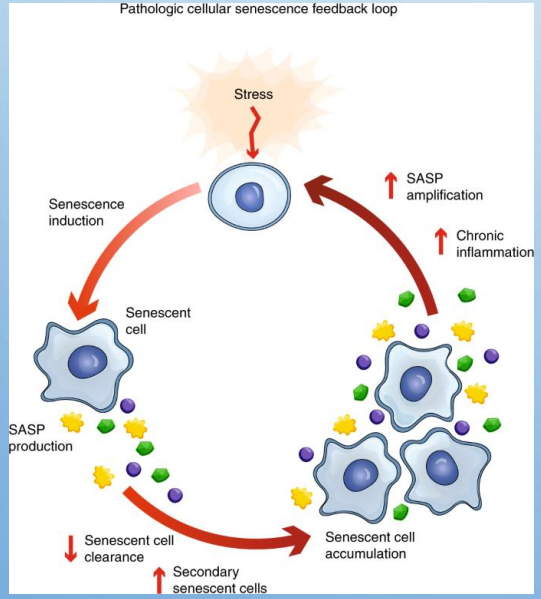
COMMON PATHWAYS OF CR, FASTING, AND MANY POLYPHENOLS EPIGENTIC ACTIVITY, ESP. SIRT PATHWAY

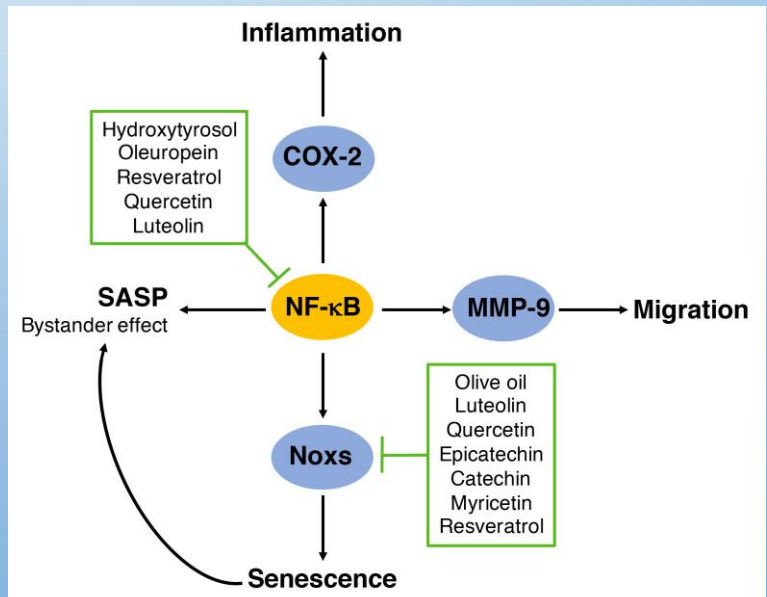




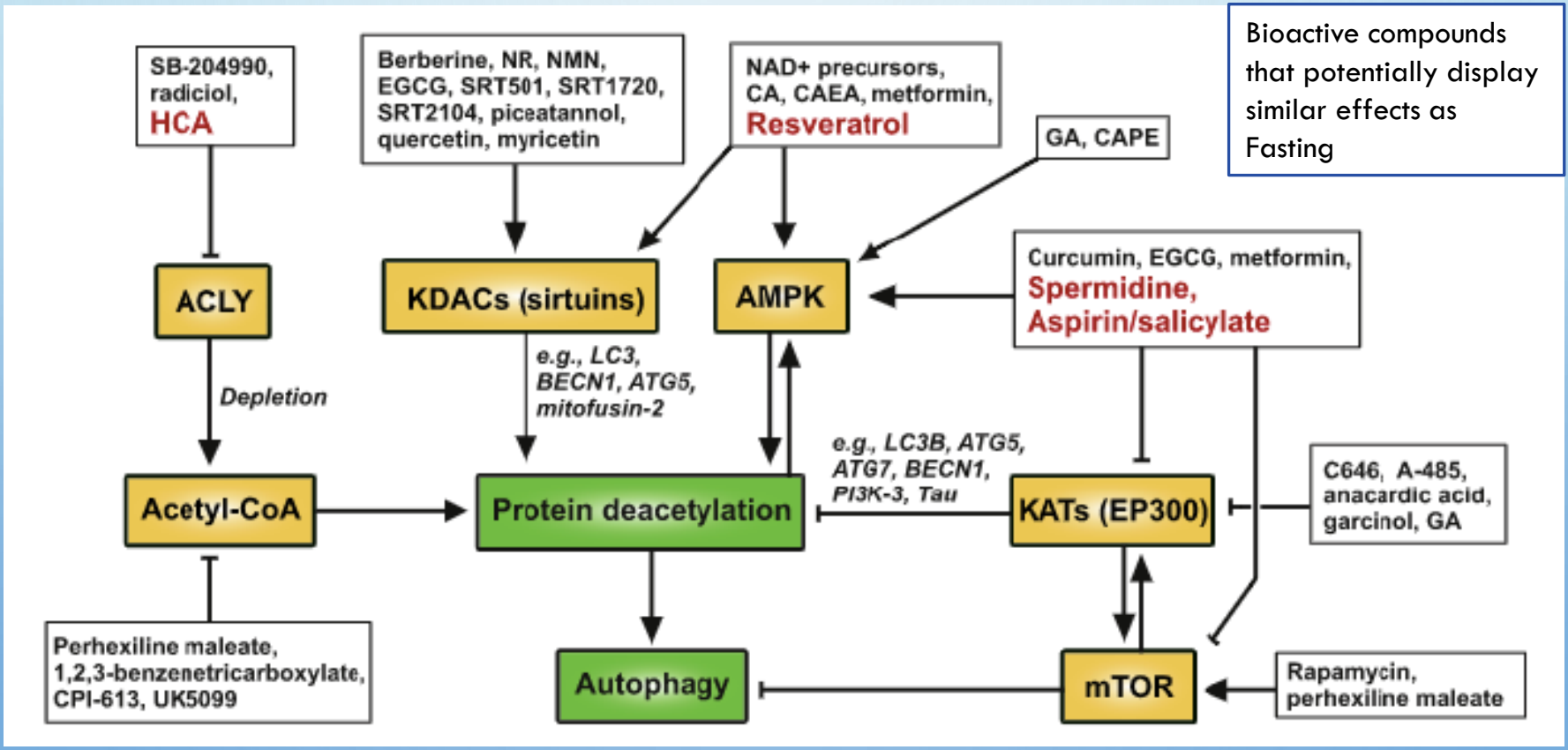
FASTING, POLYPHENOLS, SENESCENCE







FASTING MIMETICS: FROM ADDITIVES TO PHARMACEUTICS (MABS,CART T) COMBINATIONS USEFULL?



CASE STUDY: COMPARING FASTING AND A FASTING MIMETIC SIRT-FOOD SHOT: MICROBIOTA, EPIGENETICS

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 < 120 kcal/day
n: 22 in Pernegg Monastery

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

Feces, Blood spots before, after 1,3 month

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

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

STUDY SENOLYTICS, SENESCENCE MARKERS IN BRDU TREATED PRE-ADIPOCYTES, 3T3

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]

Stem Cells. Author manuscript; available in PMC 2015 Aug 19.
Published in final edited form as:
Stem Cells. 2008 Dec; 26(12): 3218–3227.
Published online 2008 Sep 18. doi: 10.1634/stemcells.2008-0299

Bromodeoxyuridine Induces Senescence

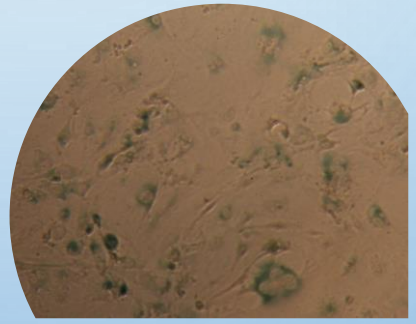
EGCG Uji-XP™

Anthocyanins-Bluezones®

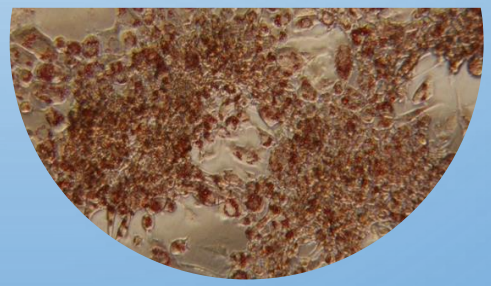
Ayurvedic Spermidine Bluezones®

BLUEZONES™ RESVERATROL

Phloretin, BHB, Butyrate (Merck)



B-Gal, senescence



Adipocytes, fat droplets

IN VITRO CONFIRMATION THAT SELECTED COMPOUNDS ARE ACTIVE IN PREADIPOCYTES, 3T3. MARKERS FOR SENESCENCE, AUTOPHAGY, EXPRESSION SIRT 3. BEST EGCG

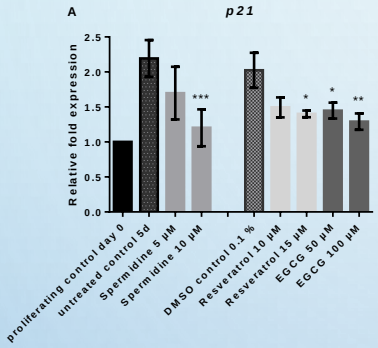
EGCG Uji-XP™

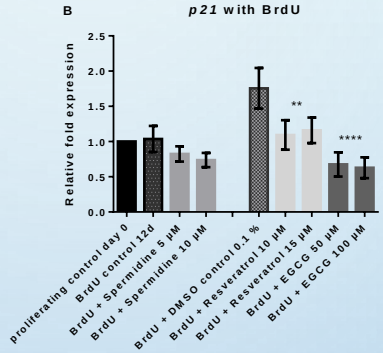
Anthocyanins-Bluezones®

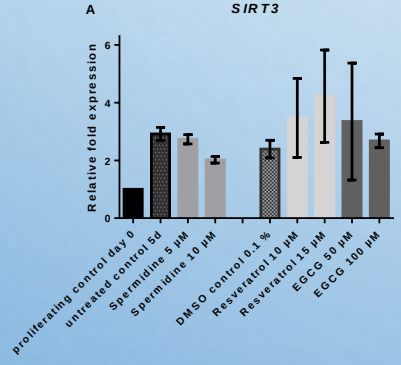
Ayurvedic Spermidine Bluezones®

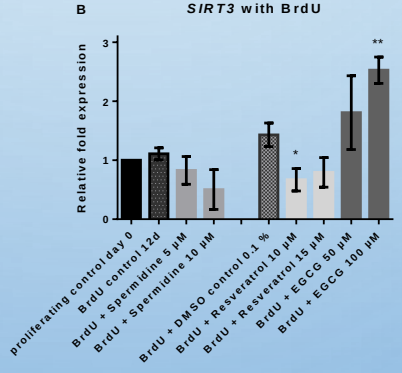
BLUEZONES™ RESVERATROL

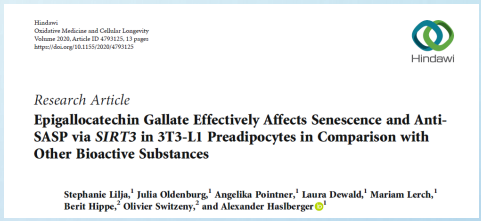
Phloretin, BHB, Butyrate (Merck)











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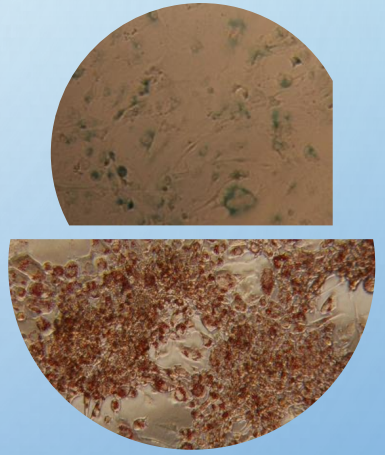
Research Article

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]



Pre, Adipocytes, fat droplets
B-Gal, senescence

BUCHINGER FASTING RESULTED IN A RISE IN THE DISTRIBUTION OF PROTEOBACTERIA, INCREASED MICROBIOTA DIVERSITY AND A SIGNIFICANT INCREASE IN CHRISTENSENELLA

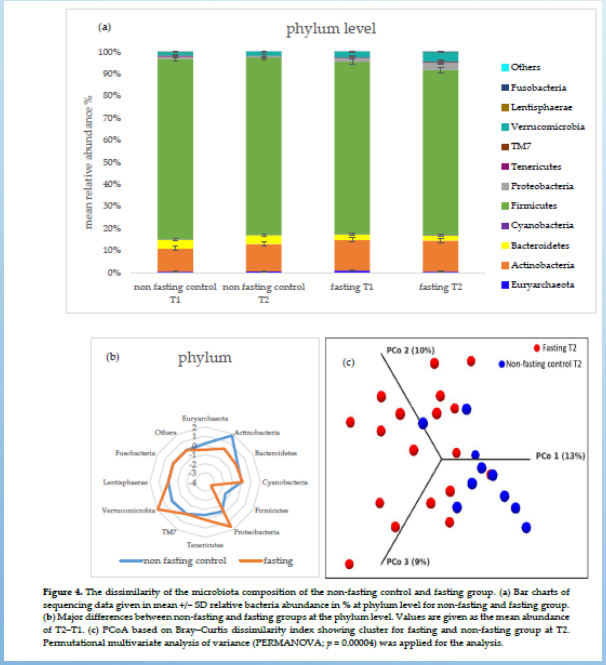


Figure 4. The dissimilarity of the microbiota composition of the non-fasting control and fasting group. (a) Bar charts of sequencing data given in mean +/- SD relative bacteria abundance in % at phylum level for non-fasting and fasting group. (b) Major differences between non-fasting and fasting groups at the phylum level. Values are given as the mean abundance of T2–T1. (c) PCoA based on Bray–Curtis dissimilarity index showing cluster for fasting and non-fasting group at T2. Permutational multivariate analysis of variance (PERMANOVA; $p = 0.00004$) was applied for the analysis.

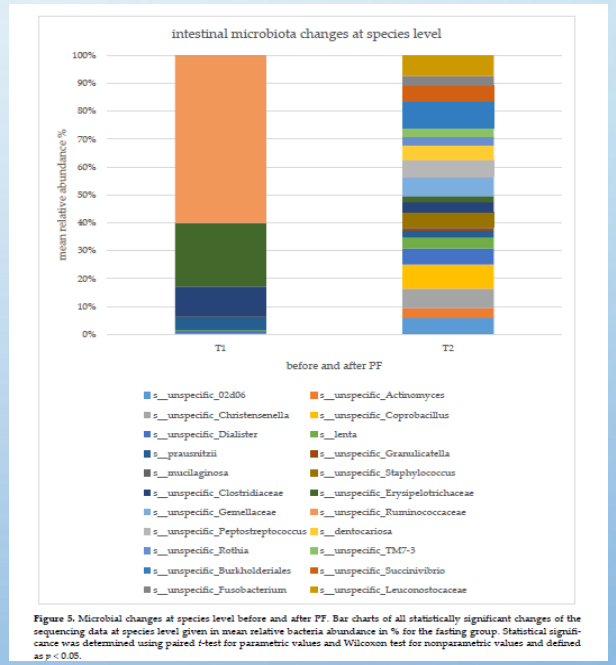


Figure 5. Microbial changes at species level before and after PF. Bar charts of all statistically significant changes of the sequencing data at species level given in mean relative bacteria abundance in % for the fasting group. Statistical significance was determined using paired *t*-test for parametric values and Wilcoxon test for nonparametric values and defined as $p < 0.05$.

3M SIRT INDUCING DRINK INCREASED *ACTINOBACTERIA*. FIRMICUTES/*BACTEROIDETES* RATIO DECREASED AND CORRELATED WITH BMI. ONLY FASTING INCREASED BUTYRATE SIGNIFICANTLY

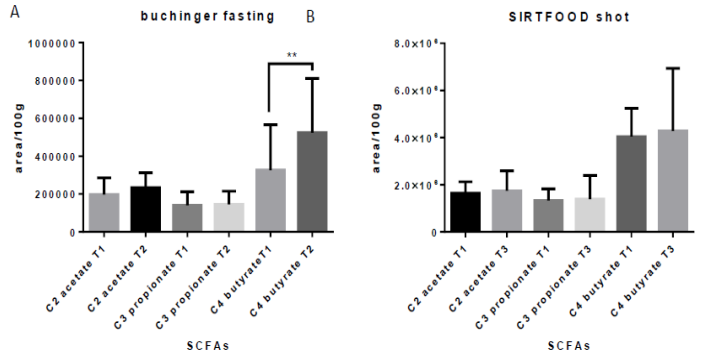


Figure 7: Amount of SCFAs produced given as area/100g stool for buchinger fasting (A) and SIRTFOOD shot (B) interventions. Statistical significance between timepoint 1 (T1) and end (T2 or T3) of the intervention was determined using paired t-test for parametric values and Wilcoxon test for nonparametric values.

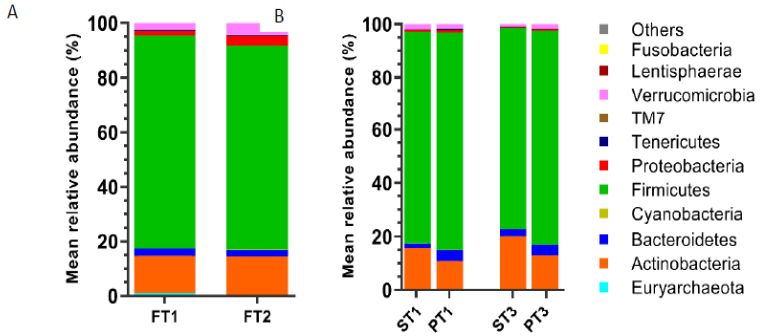


Figure 6: Abundance microbiota by phyla for fasting group (A), SIRTFOOD shot (ST1 vs ST3) (B) and placebo group (PT1 vs PT3) (B). Results are expressed in percentage of the mean of relative abundance for the different phyla. Statistical significance between timepoint 1 (T1) and end (T2 or T3) of the intervention was determined using paired t-test for parametric values and Wilcoxon test for nonparametric values.

POSITIVE CORRELATION OF THE ABUNDANCE OF BUTYRATE-PRODUCING *BACTEROIDETES* WITH MIR125, SIRT-1 EXPRESSION, TELOMERE LENGTH

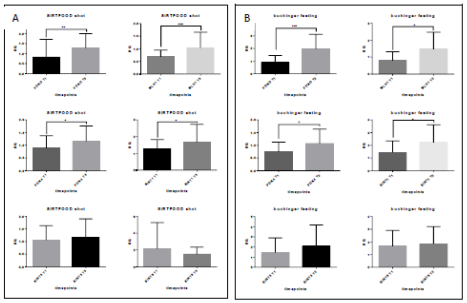


Figure 4: RQ selected mRNA gene expression (*FoxO1, MLH1, PDK4, SIRT1, SIRT3, SIRT6*) SIRTFOOD shot and buchinger fasting. The results are expressed as mean +/- SD. Statistical significance between timepoint 1 (T1) and end (T2 or T3) of the intervention was determined using paired t-test for parametric values and Wilcoxon test for nonparametric values.

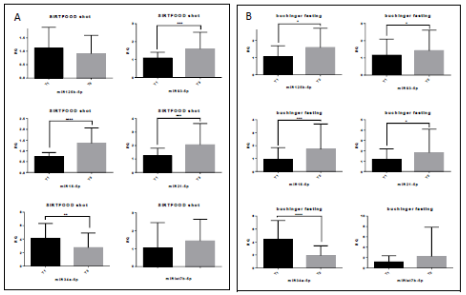


Figure 5: RQ selected miRNA gene expression (*miR125b-5p, miR93-5p, miR16-5p, miR21-5p, miR34a-5p, miRlet7b-5p*) SIRTFOOD shot and buchinger fasting. The results are expressed as mean +/- SD. Statistical significance between timepoint 1 (T1) and end (T2 or T3) of the intervention was determined using paired t-test for parametric values and Wilcoxon test for nonparametric values.

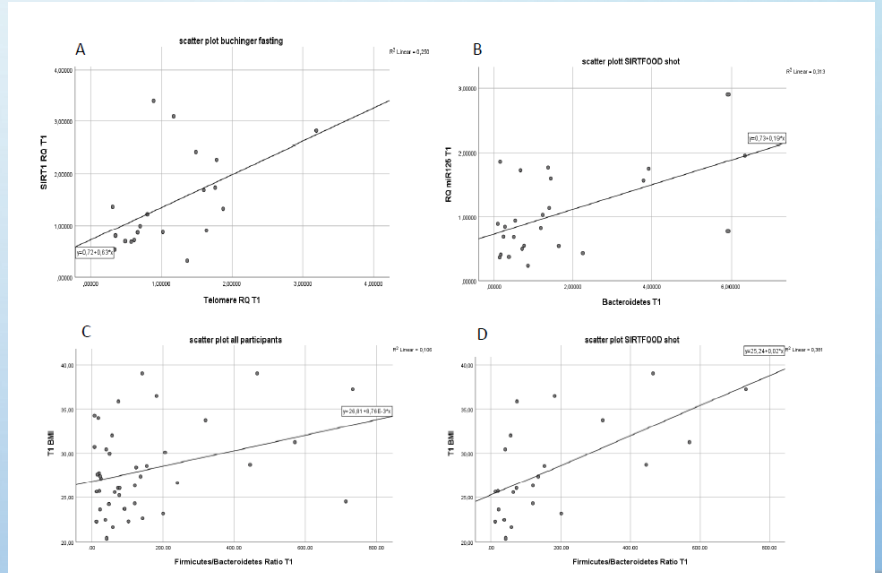
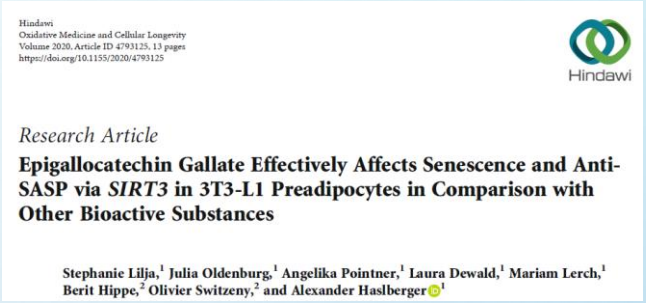


Figure 8: spss output scatter plots. (A) shows a positive correlation between telomere length and SIRT1 expression for buchinger fasting at baseline. Bacteroidetes and miR125b-5p positively correlated in the SIRTFOOD shot intervention at baseline(B). For all participants the ratio of Firmicutes/Bacteroidetes increased with higher BMI (C), which was also seen for the SIRTFOOD shot intervention Discussion (D). Statistical significance was defined as $p < 0.05$.

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

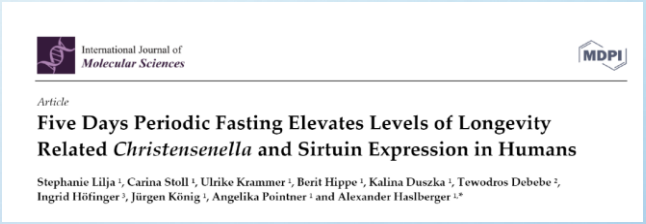

Hindawi
Oxidative Medicine and Cellular Longevity
Volume 2020, Article ID 4793125, 13 pages
https://doi.org/10.1155/2020/4793125

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

Stephanie Lilja [1], Carina Stoll [1], Ulrike Krammer [1], Berit Hippe [1], Kalina Duszka [1], Tewodros Debebe [2], Ingrid Höfinger [3], Jürgen König [1], Angelika Pointner [1] and Alexander Haslberger [1,*]

Online ISSN: 2160-3855, Print ISSN: 2378-7007

Functional Foods in Health and Disease

Home Editorial Team Iss

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

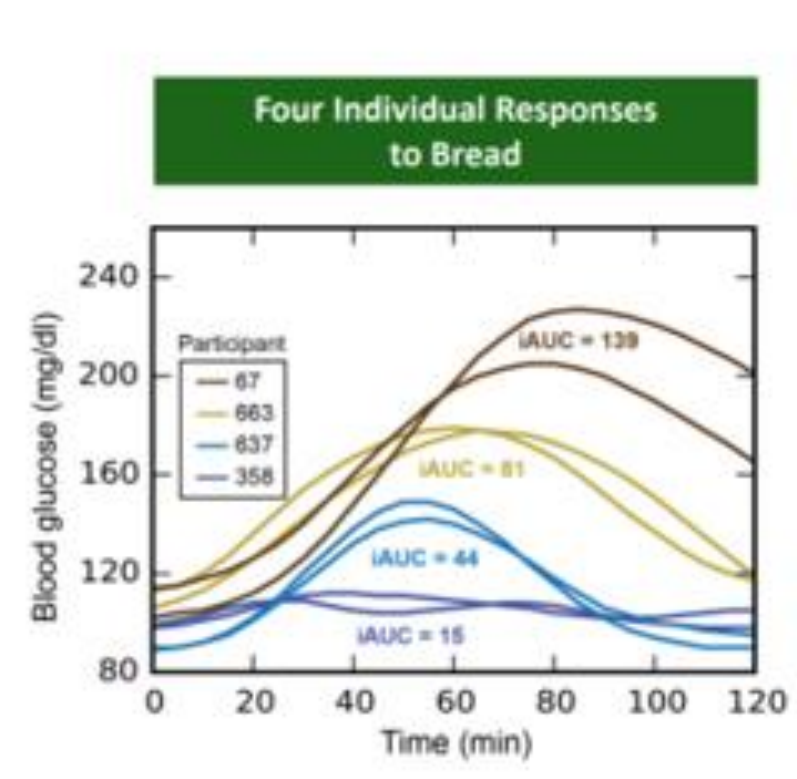
BCHD

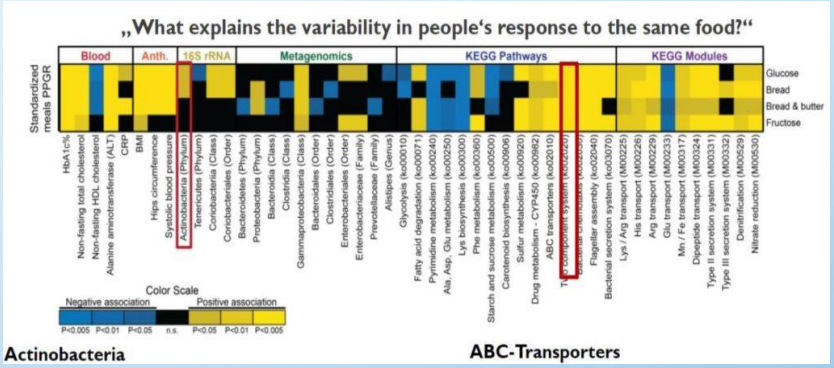
Bioactive Compounds in Health and Disease

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*

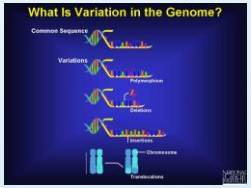
PERSONALISED NUTRITION: HIGHLY DIFFERENT PERSONAL RESPONSES TO DIETS, GLYCEMIC RESPONSES, EXPLANATIONS?

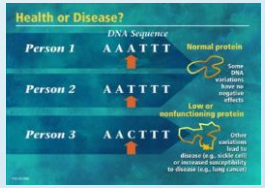


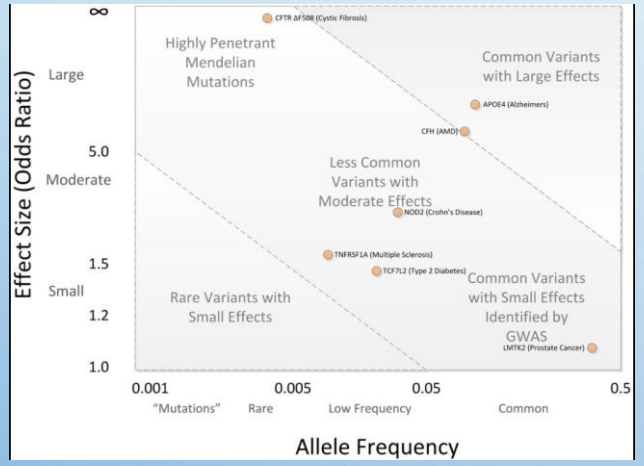


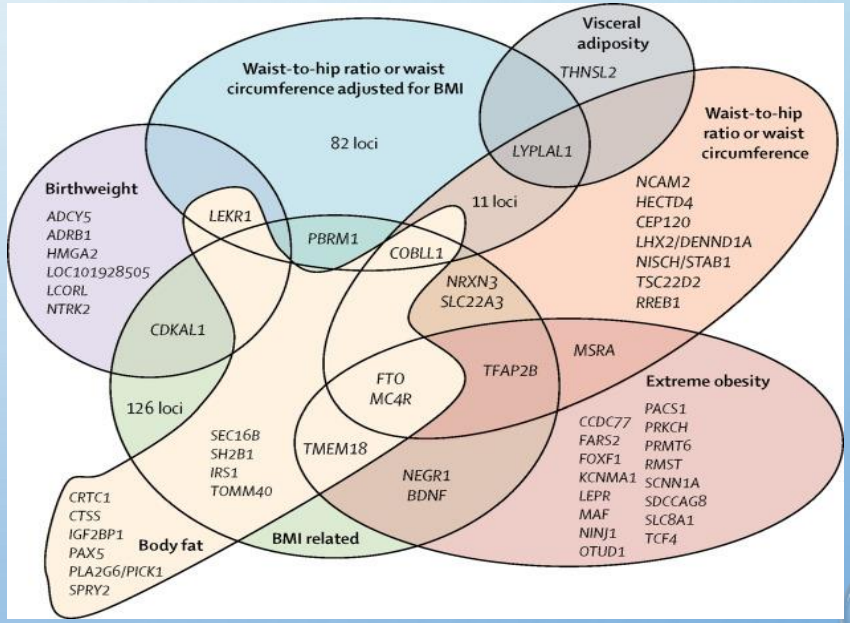
Different people have different, opposite responses to standardized meal, bread, Zeevi et al., 2015, Cell

GENETICS: GWAS : SNPS, COMMON VARIANTS HAVE OFTEN ONLY MODERATE EFFECTS









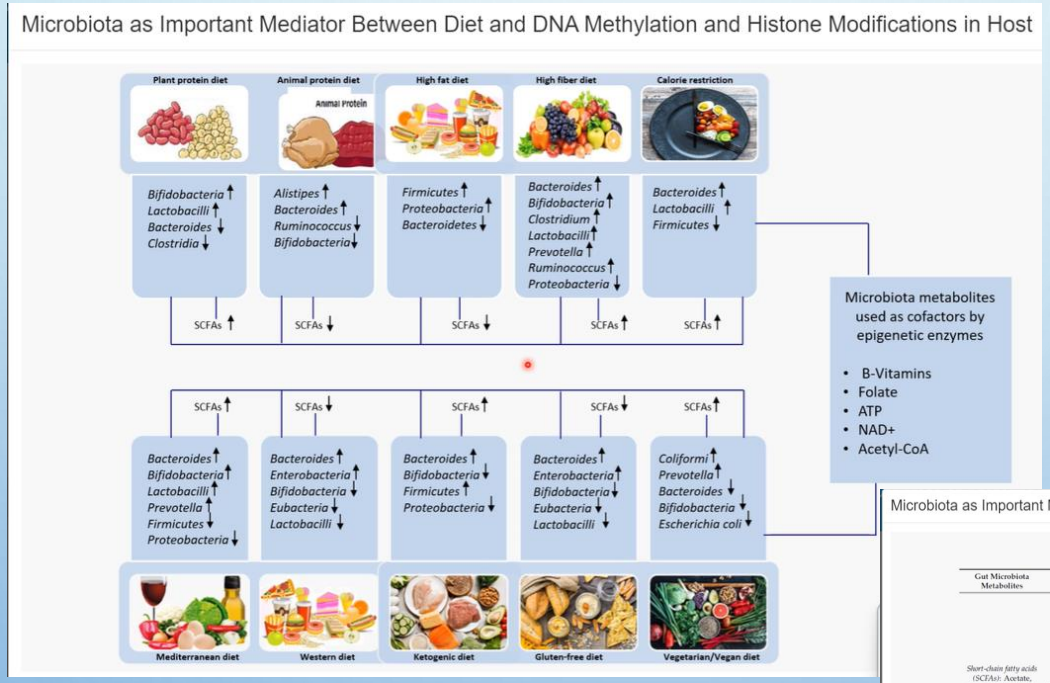
Methods

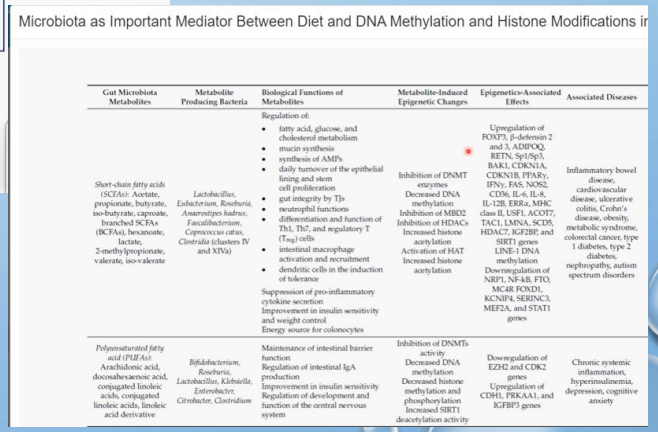
Prediction of individual genetic risk to disease from genome-wide association studies

Naomi R. Wray,[1,4] Michael E. Goddard,[2,3] and Peter M. Visscher[1]

[1]Genetic Epidemiology, Queensland Institute of Medical Research, Queensland 4029, Brisbane, Australia; [2]Faculty of Land and Food Resources, University of Melbourne, Victoria 3010, Australia; [3]Department of Primary Industries, Victoria 3049, Australia

INTERACTIONS BETWEEN DIETS, MICROBIOTA AND EPIGENETICS ARE MORE IMPORTANT, EXPERIENCE



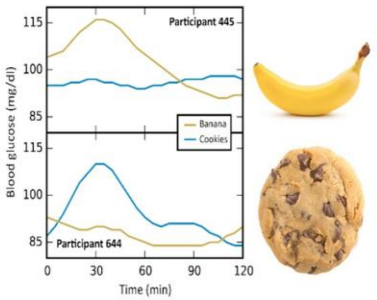


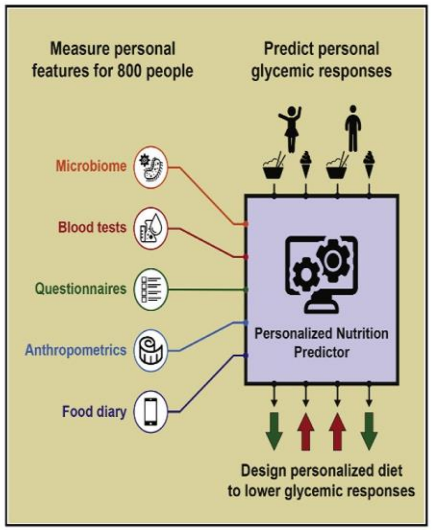
***Dina Bellizzi**, University of Calabria, Italy , **Annalisa Terranegra**, Sidra Medical and Research Center, Qatar*

CORRELATION OF MICROBIOTA STRUCTURE WITH GLYCEMIC RESPONSES USED FOR ALGORITHMS FOR DIETARY ADVICE

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

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





Mikrobiota Zusammensetzung beeinflusst Blutglucoselevel

Eran Elinav and Eran Segal, Weizmann Institute of monitoring the blood sugar, diets, and other traits of 800 people, they built an algorithm that can accurately predict how a person's blood-sugar levels will spike after eating any given meal.
They also used these personalized predictions to develop tailored dietary plans for keeping blood sugar in check.

DEFINITION OF METABOTYPES FROM GENETIC-, MICROBIOTA- BASED INFORMATION, METABOTYPING, FOOD4ME

food4me.org

Does personalised nutrition work?

Professor John Mathers, Newcastle University, UK

John Mathers leads work on the design, delivery and evaluation of outcomes from the Food4Me project's Proof-of-Principle study. He is professor of human nutrition and director of the Human Nutrition Research Centre, Newcastle University, UK.

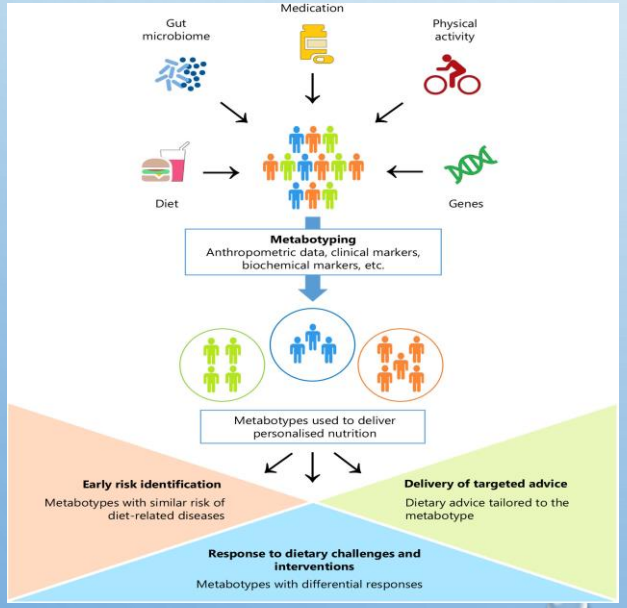
Molecular Nutrition & Food Research

Research Article | Open Access

Evaluation of the Metabotype Concept Identified in an Irish Population in the German KORA Cohort Study

Anna Riedl, Elaine Hillesheim, Nina Wawro, Christa Meisinger, Annette Peters, Michael Roden, Florian Kronenberg, Christian Herder, Wolfgang Rathmann, Henry Völzke, Martin Reincke ... See all authors

First published: 11 February 2020 | https://doi.org/10.1002/mnfr.201900918 | Citations: 1



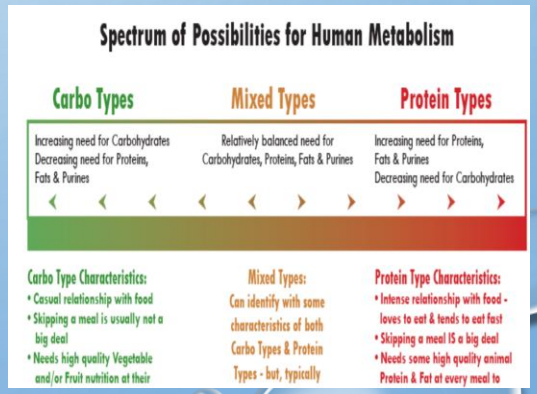
Hillesheim et al. Nutr Metab (Lond) (2020) 17:82
https://doi.org/10.1186/s12986-020-00499-z

Nutrition & Metabolism

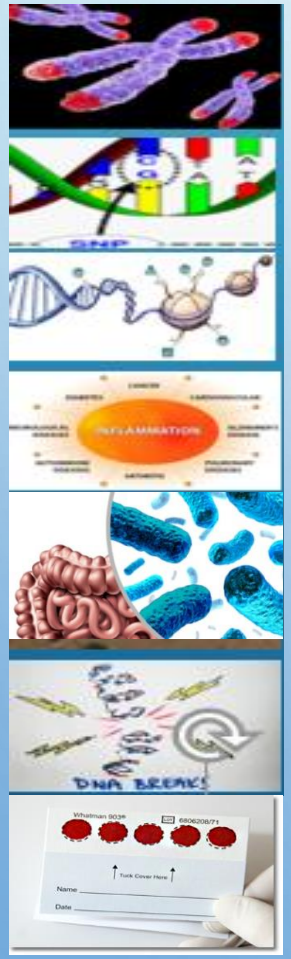
RESEARCH Open Access

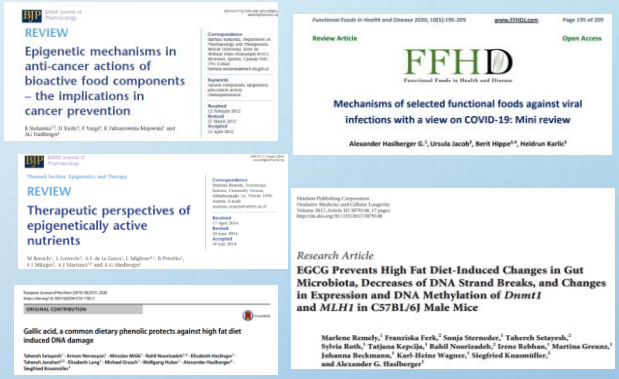
Optimisation of a metabotype approach to deliver targeted dietary advice

Elaine Hillesheim[1,2], Miriam F. Ryan[1], Eileen Gibney[1], Helen M. Roche[2,3] and Lorraine Brennan[1,2*]



Personalisation of Additives for Prevention: Monitoring basic hallmarks of health/aging.
Use of mixes of supplements, functional foods which address specific mechanisms



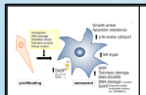
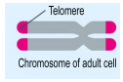
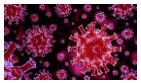


HealthBioCare GmbH

Precision Probiotics + Prebiotics with Viome's Gut Intelligence™ Test

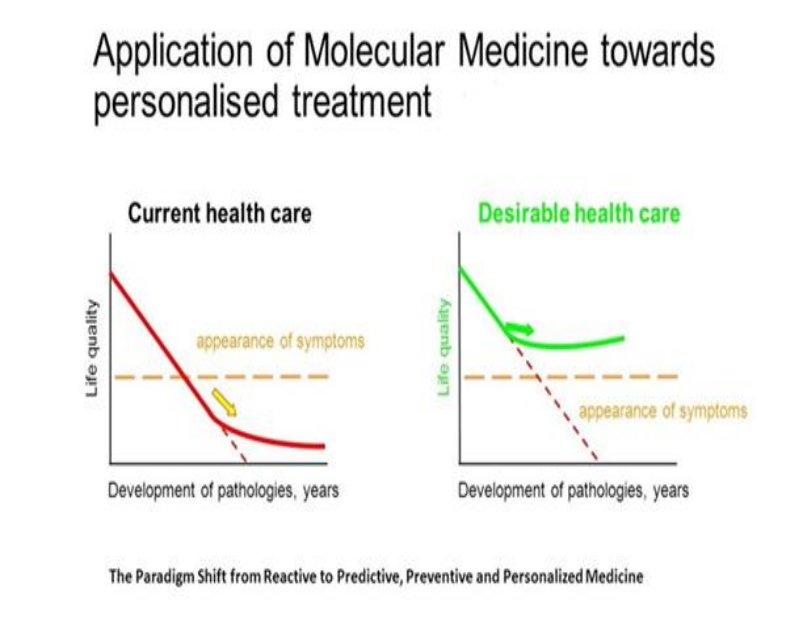
For gut health

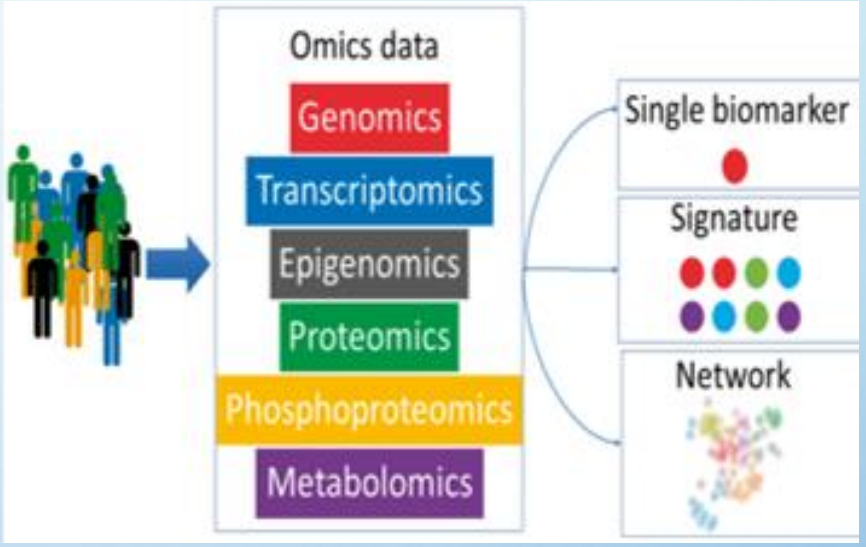
EPIGENETIC EFFECTS OF PHYTOCEUTICALS USING EPIGENETIC BIOMARKERS FOR PERSONALISED INTERVENTION

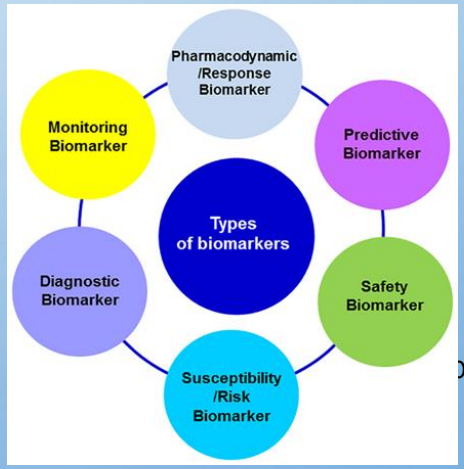
 Senescence	Oxidative Demage	 Telomere length	Inflamm-ation	epigen. Clock Methalation	Performance Fatigue	Gut Health Metabolism	Skin Hair	 Antiviral capacity	"Inflamm-Aging“	Stresss	Depression
Spermidine Curcumine Phloretine Fisetin	Sirtfoodshot Resveratrol Phloretin Fisetin Sulforaphan	Timeblock Resveratrol vegan Vit . D 3 Tocotrienole Quercetin White-Tea Extract Ginseng Grapefruit Extract Tagetes Extract Omega 3 Mix	Resveratrol Sulforaphan Tocotrienole Quercetin Curcumin Pomegranate Extract White-Tea Extract Broccoli Extract Blueberry Extract EU Apple Extract Strawberry Extract Mango Extract Omega 3 Mix Hyalurone	EGCG Vit B 12 Quercetin Folate	Virmune Tegaran Zhen Hua	Galactooligos. Sirtfood Shot Butyrate Ginseng Grapefruit Extract	Hyaluron Sirtfood Shot	EGCG Sagepolyphenols Phloretin Berberin Quercitin Resveratrol Virmune	Methionin Folsäure Sulforaphan	Butyrate Gingerol Quercetin White-Tea Extract Broccoli Extract Apple Extract Olive Leaf powder Ginseng Grapefruit Extract Tagetes Extract Omega 3 Mix	Resveratrol Curcumin White-Tea Extract Broccoli Extract Tagetes Extract Omega 3 Mix

HealthBioCare GmbH

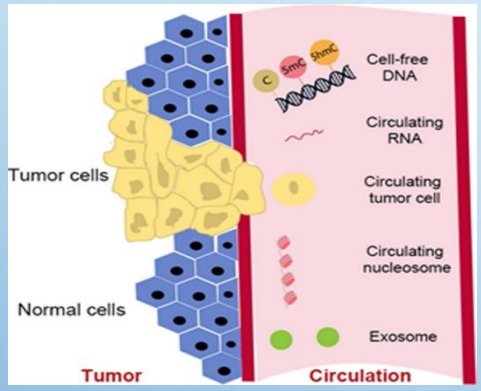
DISCUSSION: PREVENTIVE PERSONALISED (PRECISION) MEDICINE, NUTRITION NEEDS GOOD MARKERS







GOOD MARKERS: COMBINATIONS!



Haslberger 2022

cancers

MDPI

Article

Comprehensive Approach to Distinguish Patients with Solid Tumors from Healthy Controls by Combining Androgen Receptor Mutation p.H875Y with Cell-Free DNA Methylation and Circulating miRNAs

Elena Tomeva [1], Olivier J. Switzeny [1], Clemens Heitzinger [2], Berit Hippe [1,3] and Alexander G. Haslberger [3,*]

1 HealthBioCare GmbH, A-1090 Vienna, Austria; et@healthbiocare.at (E.T.); switzeny@healthbiocare.at (O.J.S.
bh@healthbiocare.at (B.H.)
2 Center for Artificial Intelligence and Machine Learning (CAIML), TU Wien, A-1040 Vienna, Austria;
clemens.heitzinger@tuwien.ac.at
3 Department of Nutritional Sciences, University of Vienna, A-1090 Vienna, Austria
* Correspondence: alexander.haslberger@univie.ac.at

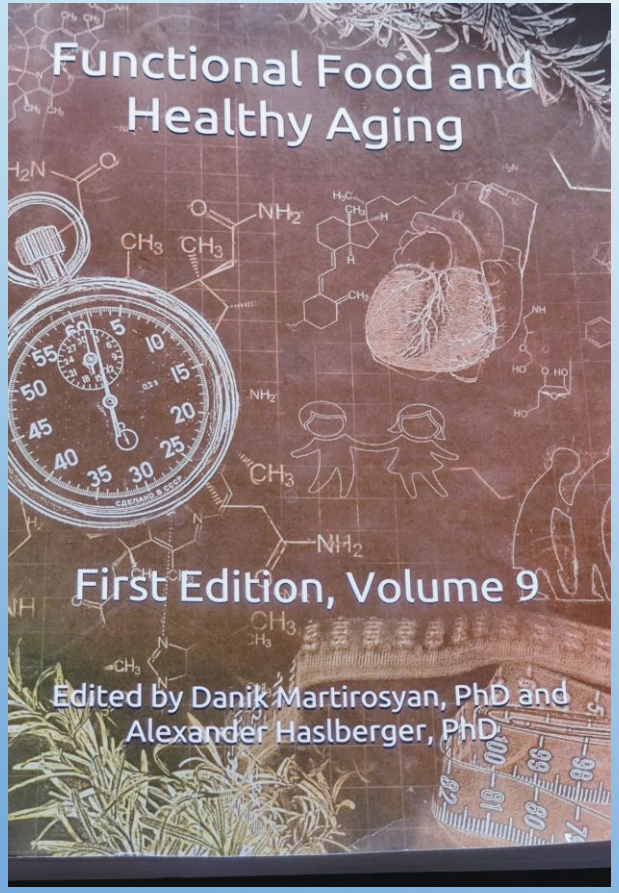
Simple Summary: Blood-based tests for cancer detection are minimally invasive and could be usefu
for screening asymptomatic patients and high-risk populations. Since a single molecular biomarke
is usually insufficient for an accurate diagnosis, we developed a multi-analyte liquid biopsy-base
classification model to distinguish cancer patients from healthy subjects. The combination of cel
free DNA mutations, miRNAs, and cell-free DNA methylation markers improved the model'
performance. Moreover, we demonstrated that the androgen receptor mutation p.H875Y is not onl
relevant in prostate cancer but had a strong predictive value for colorectal, bladder, and breast cance
Our results, although preliminary, showed that a single liquid biopsy test could detect multipl
cancer types simultaneously.

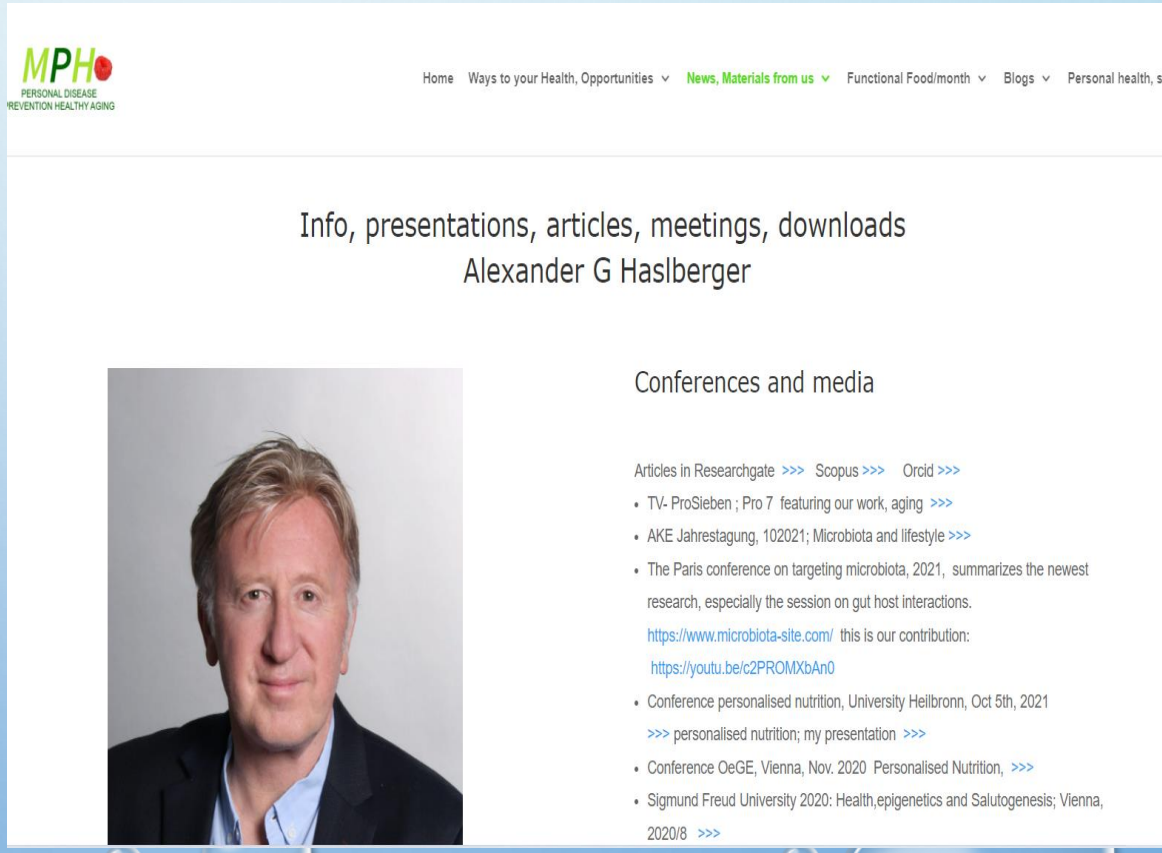
check for updates

Citation: Tomeva, E.; Switzeny, O.J.; Heitzinger, C.; Hippe, B.; Haslberger, A.G. Comprehensive Approach to Distinguish Patients with Solid

Slides and materials:

www.My-Personal.Health





COMING END OF OCTOBER 2022

Advances in Precision Nutrition, Personalization and Healthy Aging

Editor Proof

Springer

514950_1_En_BookFrontmatter ☑ TYPESET ☐ DISK ☐ LE ☑ CP Disp.:5/9/2022 Pages: ix Layout: German_T1

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