Universitätsklinikum Leipzig
Medizin ist unsere Berufung.

Darmflora und enternales Mikrobion

Hat mein Darm auch Charme?

Marc-Philipp Radosa

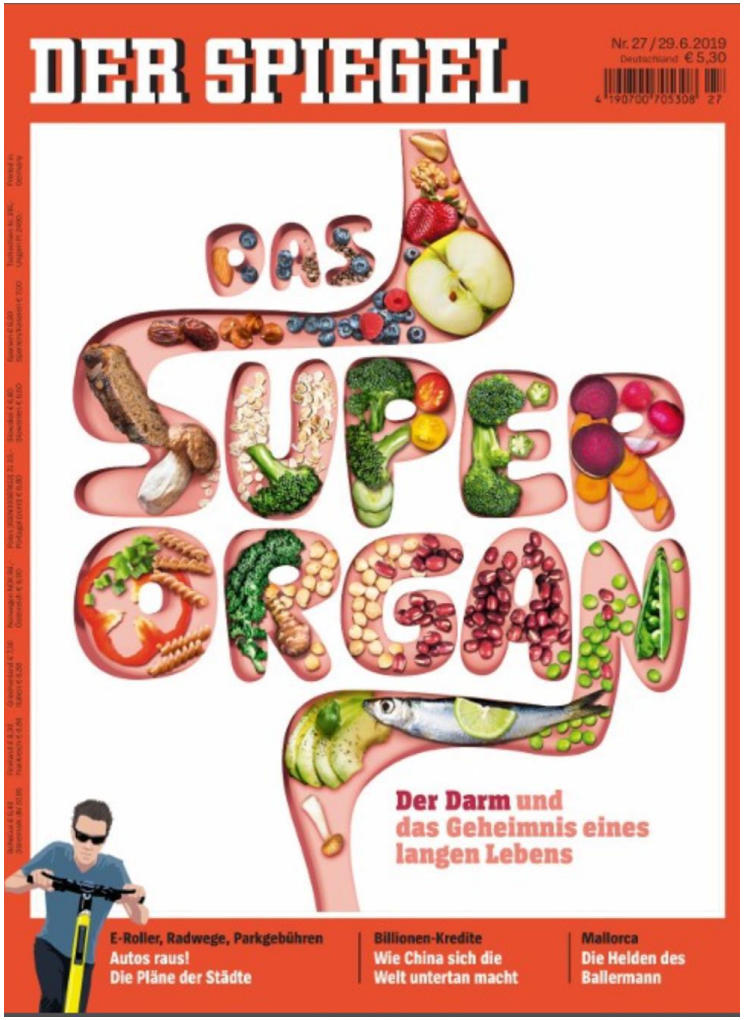
Klinik und Poliklinik für Frauenheilkunde

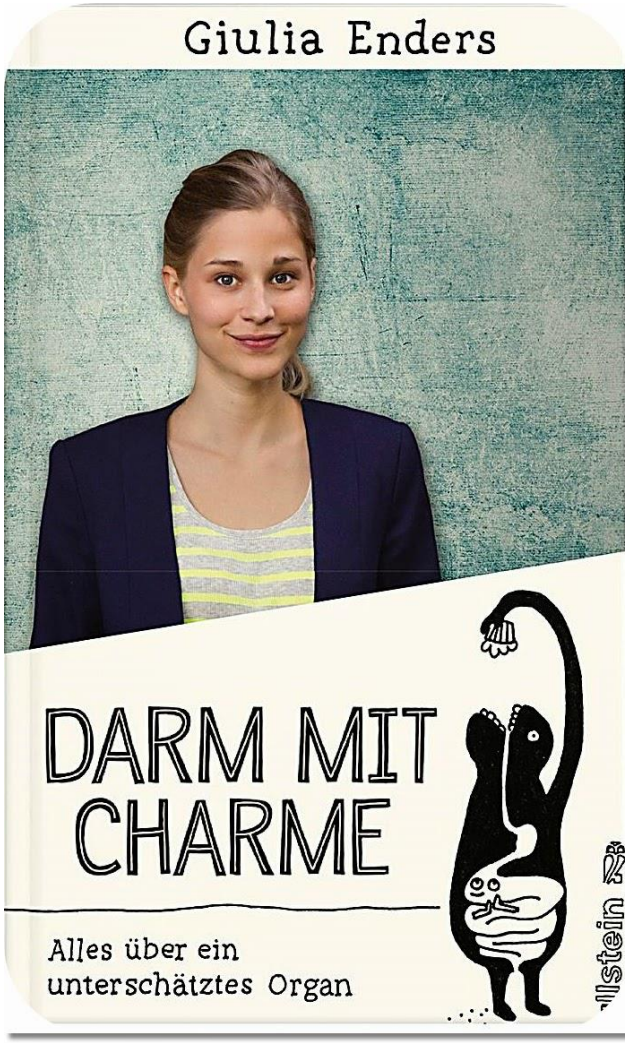
Universitätsklinikum Leipzig

Agenda

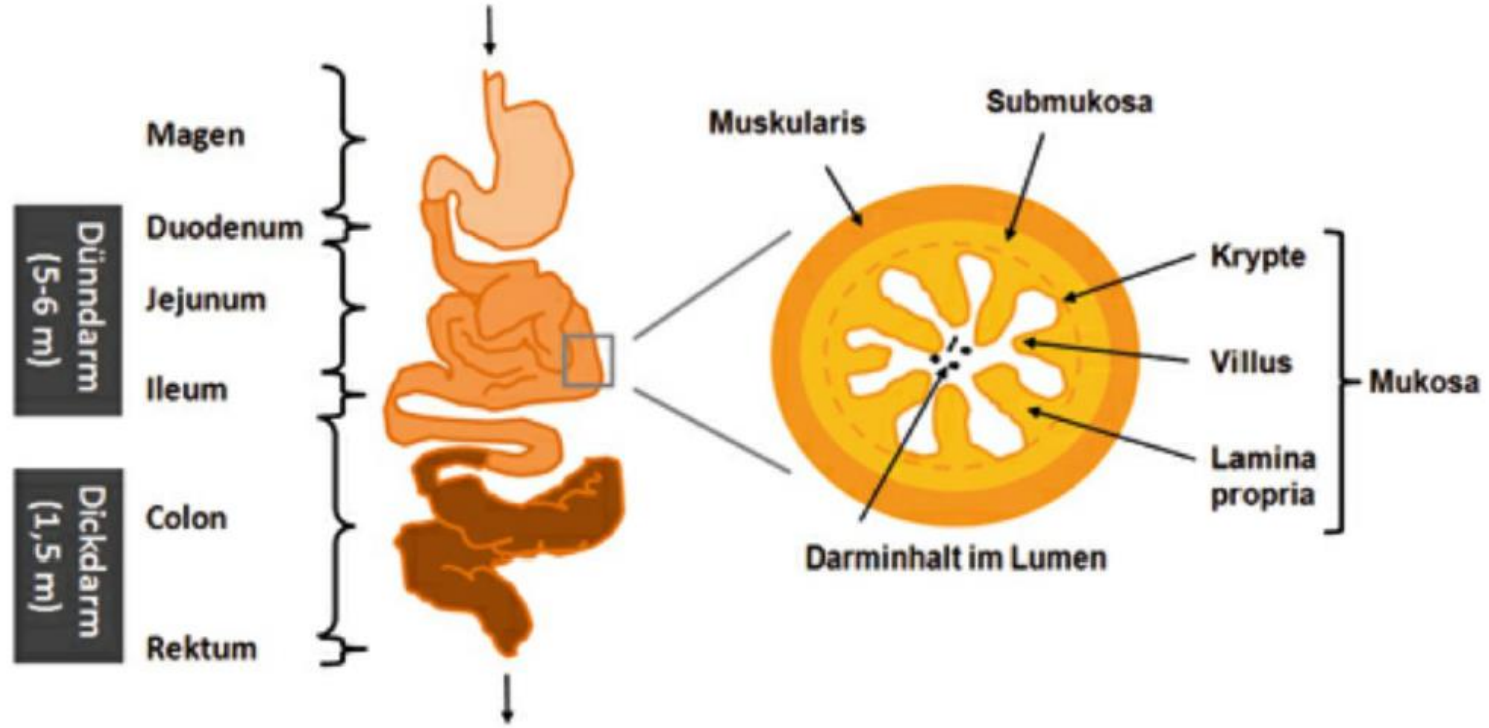
Wer ist die Darmflora und wenn ja wie viele?

Welche Erkenntnisse gibt es in der Gynäkologie zur Darmflora und Krebs


DER SPIEGEL
Nr. 27 / 29.6.2019
Deutschland € 5,30
DAS SUPER ORGAN
Der Darm und das Geheimnis eines langen Lebens
E-Roller, Radwege, Parkgebühren
Autos raus!
Die Pläne der Städte
Billionen-Kredite
Wie China sich die Welt untertan macht
Mallorca
Die Helden des Ballermann

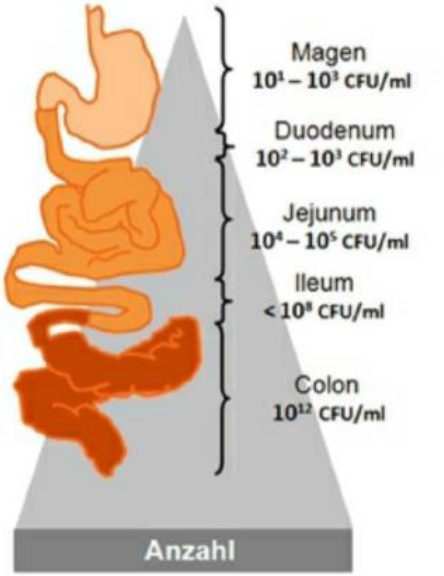

Giulia Enders
DARM MIT CHARME
Alles über ein unterschätztes Organ

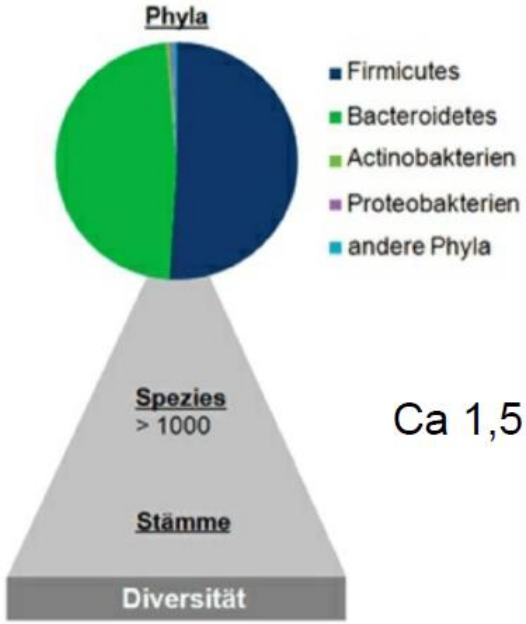
Aufbau und Funktion des Darmes



Haller et al, 2015

Die Entwicklung, Komplexität und Variabilität der intestinalen Mikrobiota





Ca 1,5 kg!

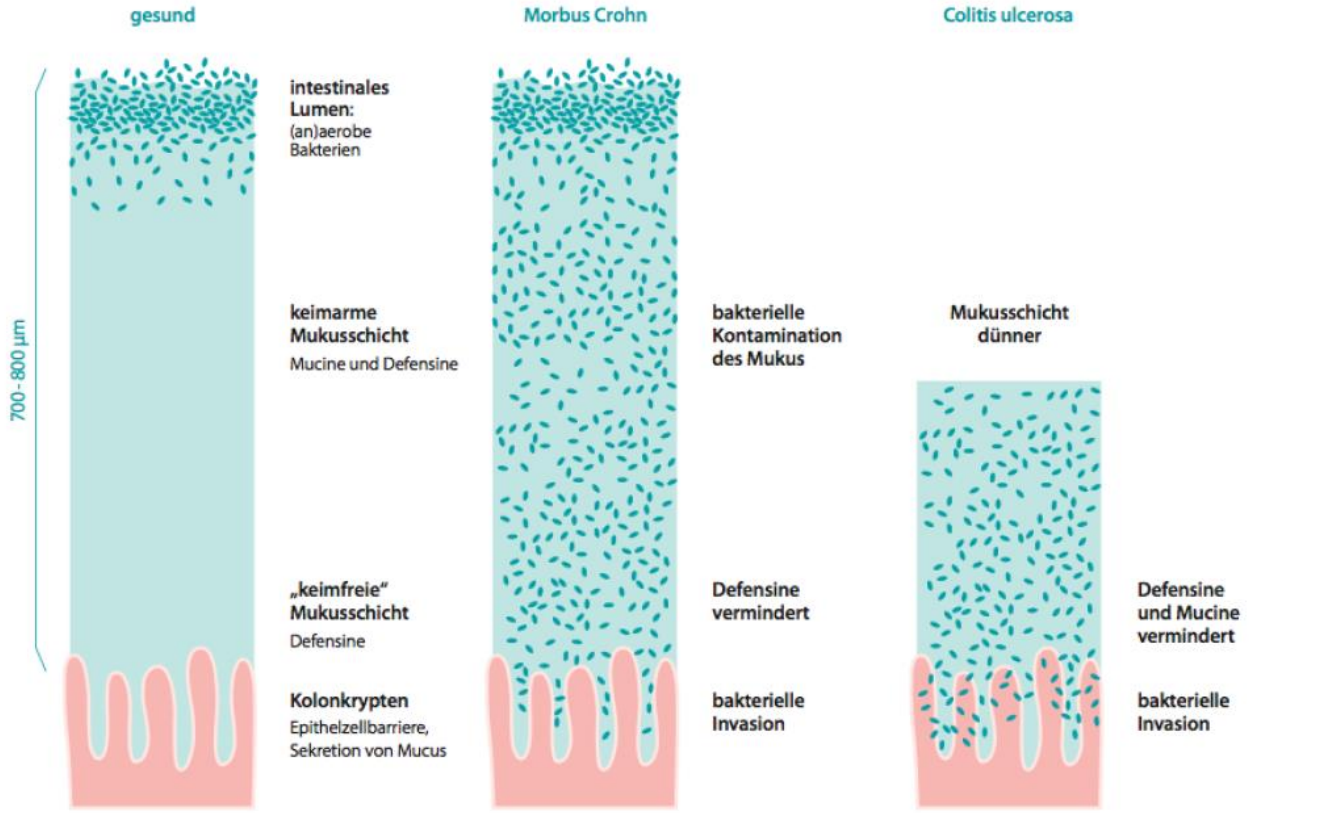
Wenig Diversität auf Phylumebene:
99% der Intestinalen Mikrobiota: Firmicutes, Bacteroides, Actinobacteria

Hohe Diversität auf Speziesebene (über 1000 Spezies)
Zusammensetzung abhängig zum Abstand zu der Mukosa

Haller et al, 2015

Mikrobiom
Begriffe

- Kolonisationsresistenz
- Immunsystem
- Nährstoffe und Vitamine
- Stuhlkonsistenz und Peristaltik



Aus Fachinfo 0113, Ganzimmun

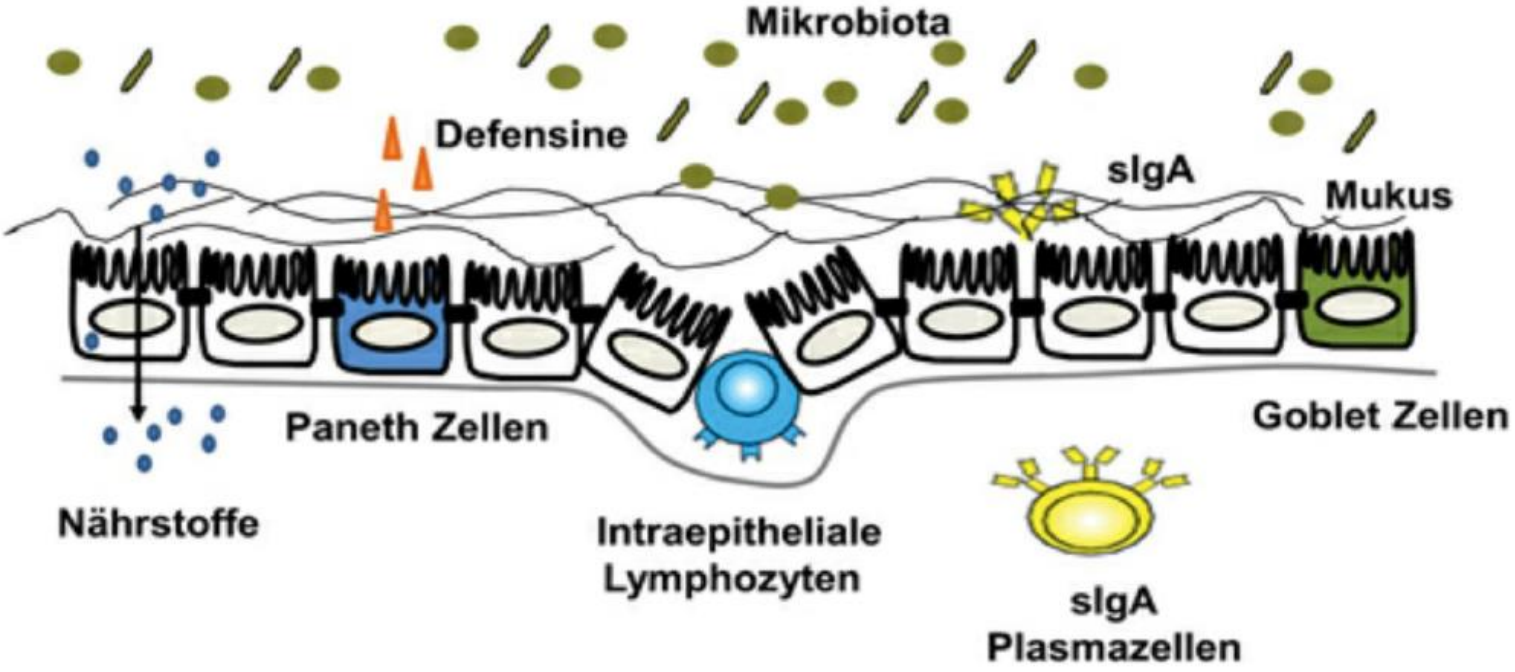
Veränderungen der Mukusschicht bei chronisch-entz. Darmerkrankungen

Kernmikrobiom: Enterotypen

- **Typ 1: v. a. Bacteroides (häufigster Typ, tierische Fette und Proteine)**
- **Typ 2: v. a. Prevotella (hoher Anteil an Kohlenhydraten und Zucker)**
- **Typ 3: v. a. Ruminococcus (Vegetarier/Veganer)**

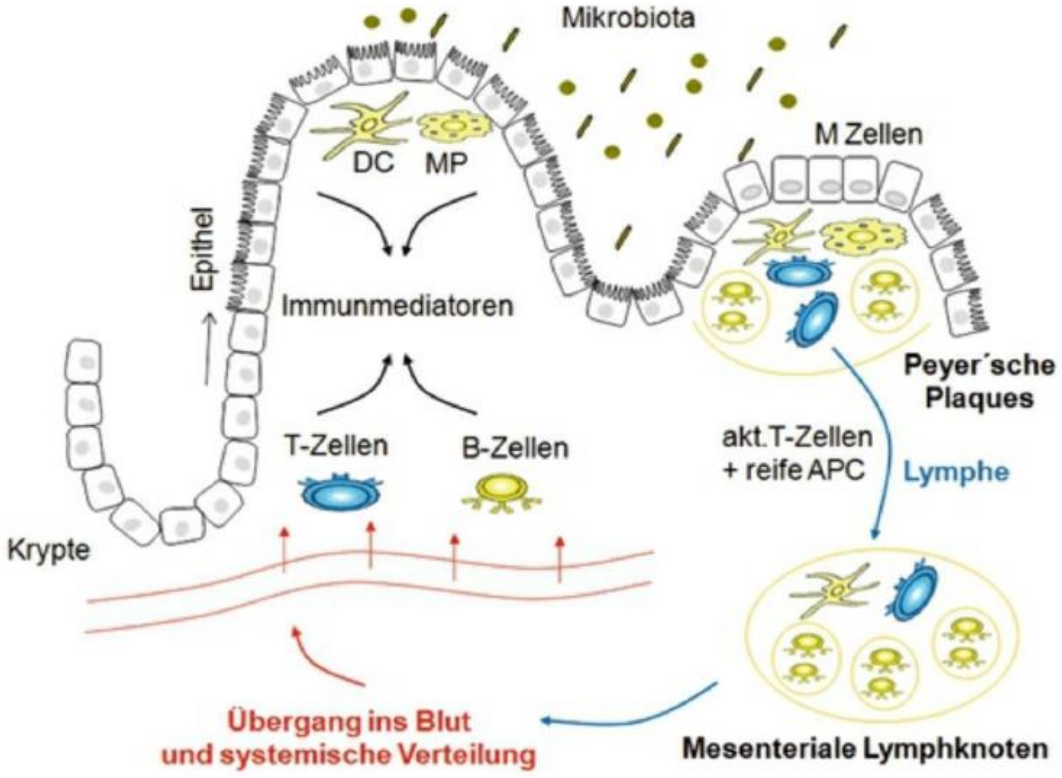
Siezen et al 2011

Selektive Darmbarriere



Haller et al, 2015

Intestinales Immunsystem und orale Toleranz, GALT = Darmassoziiertes Immunsystem



Haller et al, 2015

nature International weekly journal of science

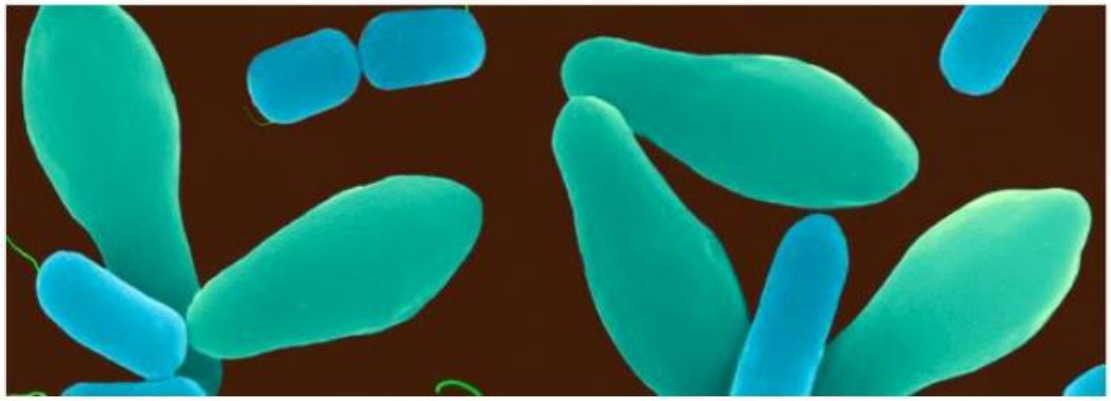
NATURE | NEWS

Gut microbes can shape responses to cancer immunotherapy

Studies find that species diversity and antibiotics influence cutting-edge treaments.

Heidi Ledford

02 November 2017



Mikrobiom und Checkpoint-Inhibition

- Antibiotikagabe vor Therapie verschlechtert Ansprechen (Ipilimumab), Akkermansia muciniphila ist protektiv (Zitvogel et al. 2015)
- Bei PDL-1 Respondern höhere Diversität, mehr Ruminococcusarten (Gopalakrishan et al., 2016)
- Transplantation von Akkermansia muciniphila verbessert Ansprechen (Routy, 2018, Wargo 2017)
- Deutliche pos. Korrelation von T-Killerzell-Infiltraten im Tumorgewebe und Ruminococcusvorkommen in der Darmflora. Negative Korrelation bei Bacteroides (Wargo et al.2017)

Pathomechanismus der zytostatikaassoziierten Diarrhoe

- Klassische Chemotherapeutika (Mucositis durch direkte Affektion von Epithelzellen des unteren GIT, Dysmotilität und Ausschüttung sekretorischer Faktoren)
- zielgerichtete Substanzen wie Antikörper und TKI (Pathomechanismus weitgehend unbekannt)
- Abhängig von Therapieregime, Komorbidität, individuelle Begleitfaktoren
- AWMF-Leitlinie

6.5.1.12. Synbiotika

6.13.	Evidenzbasierte Empfehlung
Empfehlungsgrad **0**	Eine Prophylaxe der Tumortherapie induzierten Diarrhoe mit Synbiotika kann bei immunkompetenten Patienten erwogen werden.
Level of Evidence **1b-**	Literatur: (Osterlund, Ruotsalainen et al. 2007)
Abstimmung im Plenum	Konsens

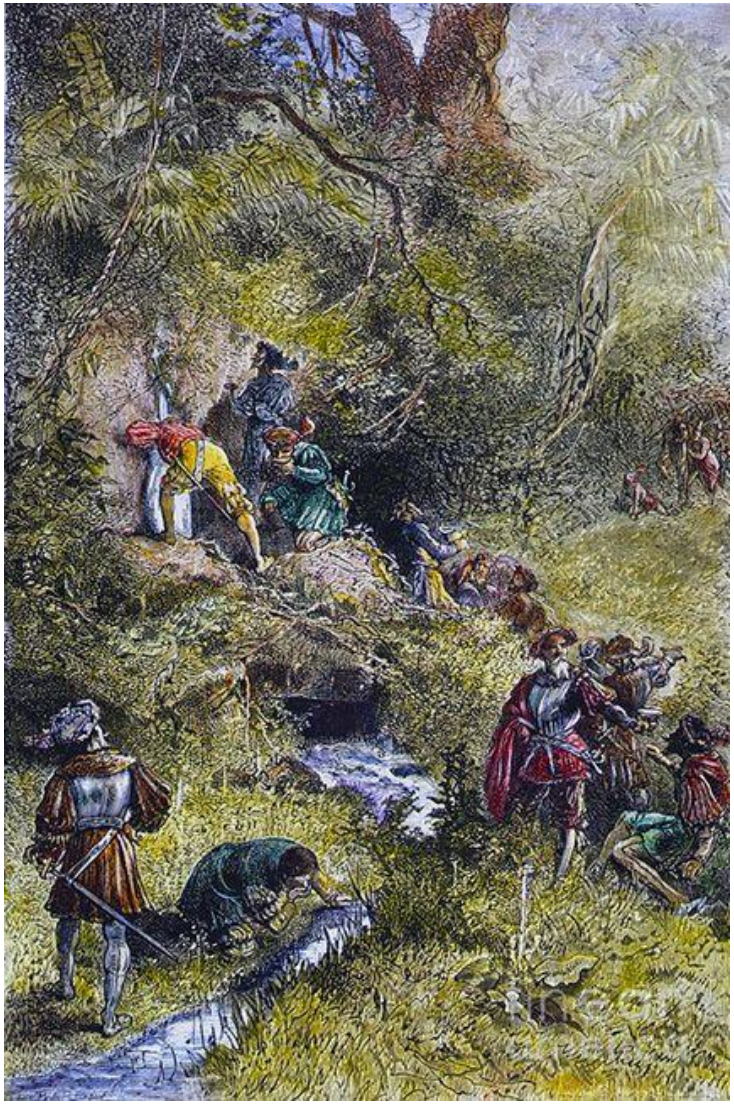
Praktische Ernährungsempfehlungen

Substrate, die ein physiologisches Mikrobiom begünstigen	**Ballaststoffe (Präbiotika) wie** ■ Flohsamenschalen ■ Leinsamen ■ Akazienfaser ■ Weizenkleie ■ resistente Stärke (z.B. resistentes Dextrin) ■ Fructo-/Galaktooligosaccaride ■ Amylopektin ■ Citruspektin ■ Vollkornhirse ■ Buchweizen ■ Erdmandeln ■ Baobab (afrikanischer Affenbrotbaum) **Sekundäre Pflanzeninhaltsstoffe aus der Gruppe der Polyphenole wie** ■ Epicatechin/Catechin (grüner Tee) ■ Procyanidine (rote Trauben) ■ Flavanole (Kakao) ■ Tannine (Tee)
Substrate, die ein unphysiologisches Mikrobiom begünstigen	■ Eiweiß in zu hohen Mengen (unabhängig von der Quelle; auch Entzündungseiweiß steht der putriden Flora als Substrat zur Verfügung) ■ Fett in zu hohen Mengen ■ raffinierte Kohlenhydrate/Stärke

Zusammenfassung

- Intaktes Mikrobiom wichtiger Gesundheitsfaktor
- Onkologische Patienten sollten entsprechend beraten werden
- Hohe Diversität und bestimmte Spezies vorteilhaft (Ruminococcusarten, Akkermansia muciniphila)
- Mikrobiomzusammensetzung Prädiktor für Therapieansprechen?
- Ausblick: Durch selektive Beeinflussung der Darmflora (z.B. durch Prä- und Probiotika, Fäkaltransplantation) neue präventive und therapeutische Ansätze werden intensiviert beforscht

Welche Erkenntnisse gibt es in der Gynäkologie zu Mikrobiom und Krebs



Komplementäre Medizin und gynäkologische Tumoren

Swisher EM, Cohn DE, Goff BA, et al. Use of complementary and alternative medicine among women with gynecologic cancers. Gynecol Oncol 2002;84:363–367

TABLE 3
Reasons Given for Using Complementary and Alternative Therapy

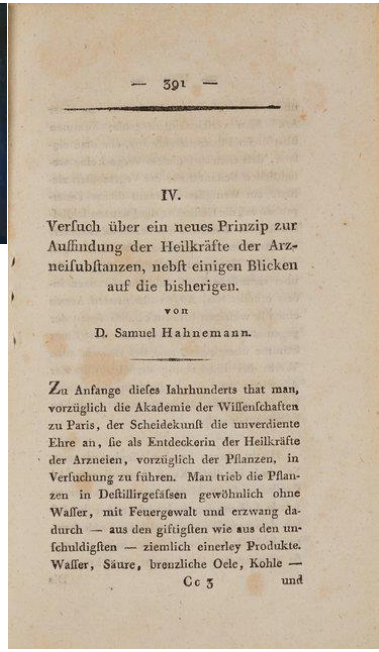
	Reason given for using CAM (%)	Perceived benefit from CAM (%)	*P* value
Directly fight the cancer with CAM	9 (36)	1 (7)	0.004
Increase the body's ability to fight cancer	16 (64)	2 (22)	0.005
Improve physical well-being	11 (44)	10 (34)	NS
Improve emotional well being, provide hope, increase optimism, etc.	15 (60)	18 (67)	NS
Counteract ill effects from the cancer or medical treatment	6 (24)	6 (22)	NS
"Might help, can't hurt"	8 (32)		
To do everything possible to fight the cancer	16 (64)		
No benefit		1 (4)	
Total	25	27	

TABLE 4
Information Sources for Users of CAM

Source of information regarding CAM	Number (%)[a]
The media (TV, magazines, newspapers)	24 (54.5)
Internet	10 (22.7)
Friends	33 (75.0)
Family	15 (43.1)
Religious contacts	13 (29.5)
Practitioners of alternative therapy	8 (18.2)
Medical doctor	3 (6.8)
Nurse	4 (9.1)
Other	3 (6.8)
Total	44

89% aller gynäkologischen onkologischen Patientinnen wünschen sich medizinische Beratung zu komplementärer Medizin

Komplementäre Medizin - Evidenzgewinnung



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IV.

Verſuch über ein neues Prinzip zur Auffindung der Heilkräfte der Arzneiſubſtanzen, nebſt einigen Blicken auf die bisherigen.

von

D. Samuel Hahnemann.

Zu Anfange dieſes Jahrhunderts that man, vorzüglich die Akademie der Wiſſenſchaften zu Paris, der Scheidekunſt die unverdiente Ehre an, ſie als Entdeckerin der Heilkräfte der Arzneien, vorzüglich der Pflanzen, in Verſuchung zu führen. Man trieb die Pflanzen in Deſtillirgefäſsen gewöhnlich ohne Waſſer, mit Feuergewalt und erzwang dadurch — aus den giftigſten wie aus den unſchuldigſten — ziemlich einerley Produkte. Waſſer, Säure, brenzliche Oele, Kohle —

Cc 3 und

Von der Expertenthese zur Evidenz

Es scheint das unselige Hauptgeschäft der alten Medicin zu sein, die Mehrzahl der Krankheiten, durch Hinzufügung neuer, zerstörender Arzneikrankheiten, wo nicht tödtlich, doch wenigstens unheilbar zu machen

Komplementäre Medizin - Evidenzgewinnung

Von der Expertenthese zur Evidenz

Randomisiert, kontrolliert, multizentrisch

Klinische Studien

Präklinische Studien

Epidemiologische Studien

Hypothese

Ernährung und Tumorgenese

Ovarialkarzinomentstehung und Ernährungsstil

Merritt MA, Tzoulaki I, van den Brandt PA, et al.
Nutrient-wide association study of 57 foods/nutrients and epithelial ovarian cancer in the European Prospective Investigation into Cancer and Nutrition study and the Netherlands Cohort Study.
Am J Clin Nutr 2016;103:161–167

Objective: We used a nutrient-wide association study approach to systematically test the association between dietary factors and invasive EOC risk while accounting for multiple hypothesis testing by using the false discovery rate and evaluated the findings in an independent cohort.

Design: We assessed dietary intake amounts of 28 foods/food groups and 29 nutrients estimated by using dietary questionnaires in the EPIC (European Prospective Investigation into Cancer and Nutrition) study (n = 1095 cases). We selected 4 foods/nutrients that were statistically significantly associated with EOC risk when comparing the extreme quartiles of intake in the EPIC study (false discovery rate = 0.43) and evaluated these factors in the NLCS (Netherlands Cohort Study; n = 383 cases). Cox regression models were used to estimate HRs and 95% CIs.

Ernährung und Tumorgenese

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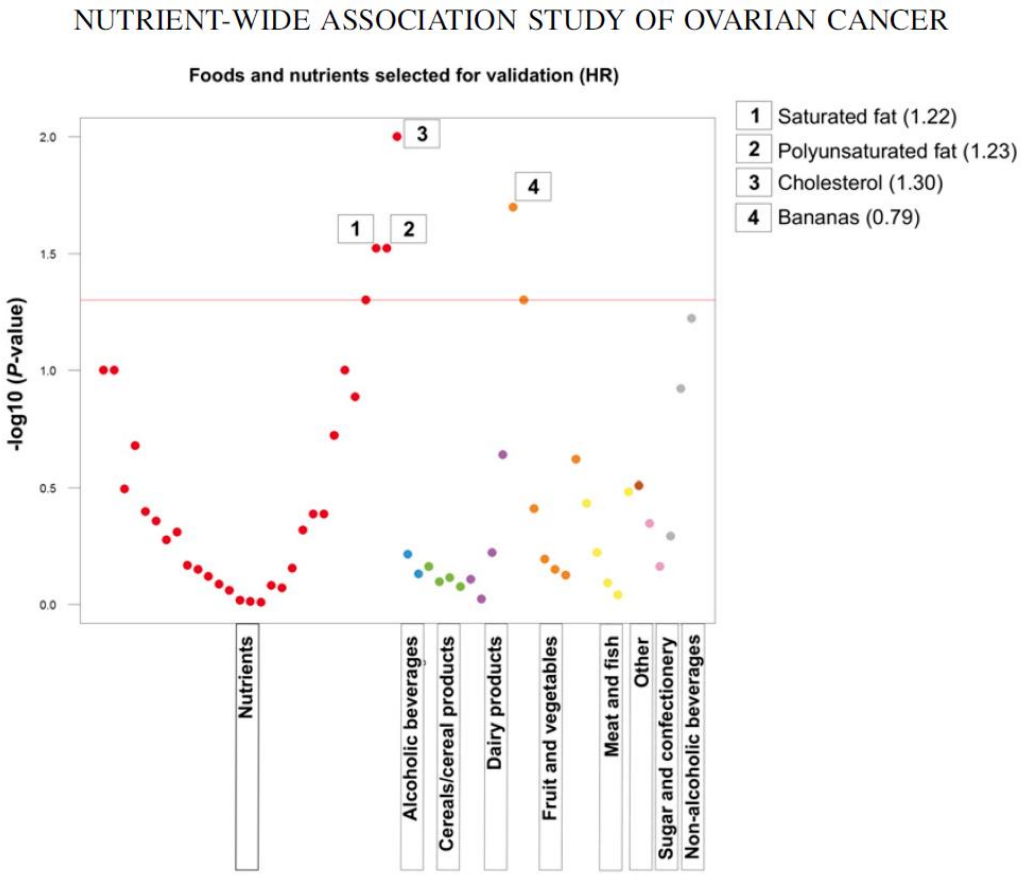

Ernährung und Tumorgenese

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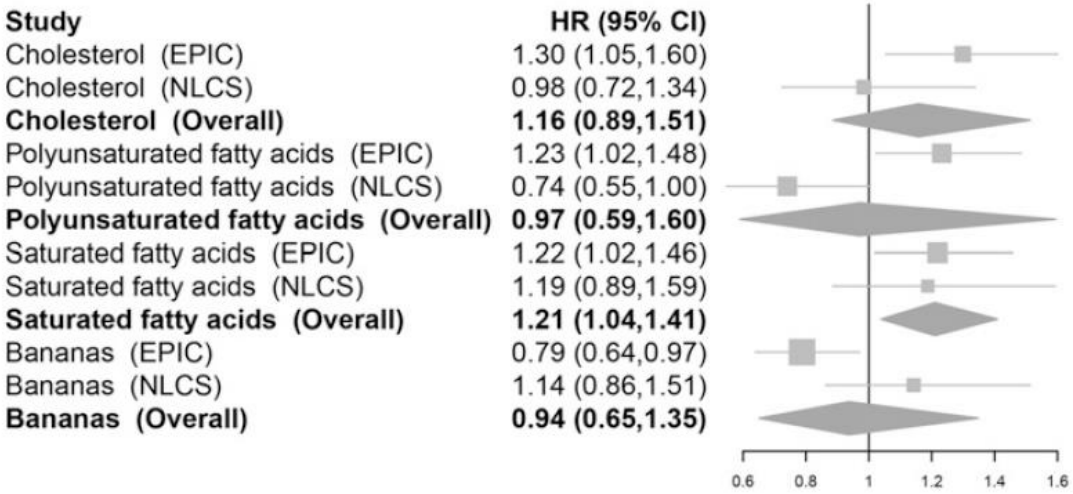

Results: None of the 4 dietary factors that were associated with EOC risk in the EPIC study (cholesterol, polyunsaturated and saturated fat, and bananas) were statistically significantly associated with EOC risk in the NLCS; however, in meta-analysis of the EPIC study and the NLCS, we observed a higher risk of EOC with a high than with a low intake of saturated fat (quartile 4 compared with quartile 1; overall HR: 1.21; 95% CI: 1.04, 1.41).

Ernährung und Tumorgenese

Selen zur Ovarialkarzinomprävention

Supplemental Selenium May Decrease Ovarian Cancer Risk in African-American Women[1–3]

Paul D Terry,[4]* Bo Qin,[5] Fabian Camacho,[6] Patricia G Moorman,[7] Anthony J Alberg,[8] Jill S Barnholtz-Sloan,[9] Melissa Bondy,[10] Michele L Cote,[11] Ellen Funkhouser,[12] Kristin A Guertin,[6] Edward S Peters,[13] Ann G Schwartz,[11] Joellen M Schildkraut,[6] and Elisa V Bandera[5]

[4]Department of Medicine, Graduate School of Medicine, University of Tennessee Medical Center, Knoxville, TN; [5]Department of

J Nutr 2017;147:621–7

Background: To our knowledge, no previous study has evaluated the associations of antioxidant intake with the risk of ovarian cancer in African-American women, who are known to have high mortality from the disease.

Objective: We sought to evaluate these associations among 406 ovarian cancer cases and 632 age- and site-matched controls of African-American descent recruited from AACES (African American Cancer Epidemiology Study), a population-based, case-control study in 11 geographical areas within the United States.

Methods: Multivariable logistic regression models were used to estimate ORs and 95% CIs adjusted for a wide range of potentially confounding factors, including age, region, education, parity, oral contraceptive use, menopause, tubal ligation, family history, body mass index (BMI), smoking status, total energy, and physical activity.

Ernährung und Tumorgenese

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TABLE 2 The association of dietary and supplemental intake of selenium with ovarian cancer, African American Cancer Epidemiology Study, 2010–2014[1]

Intake, μg/d	Cases	Controls	OR[2] (95% CI)	*P*-linear[3]
Dietary				0.1
Q1 (<47.8)	88 (21.7)	158 (25.0)	1.00 Referent	
Q2 (47.8–72.6)	122 (30.0)	158 (25.0)	1.19 (0.74, 1.91)	
Q3 (72.7–111.7)	102 (25.1)	158 (25.0)	0.98 (0.54, 1.78)	
Q4 (>111.7)	94 (23.2)	158 (25.0)	0.66 (0.31, 1.37)	
Supplemental				0.04
T1 (nonconsumer)	203 (50.0)	274 (43.4)	1.00 Referent	
T2 (0–20.0)	139 (34.2)	211 (33.4)	0.89 (0.66, 1.21)	
T3 (>20.0)	64 (15.8)	147 (23.3)	0.67 (0.46, 0.97)*	
Total				0.1
Q1 (<60.9)	110 (27.1)	158 (25.0)	1.00 Referent	
Q2 (60.9–96.4)	120 (29.6)	158 (25.0)	0.91 (0.60, 1.38)	
Q3 (96.5–137.4)	76 (18.7)	158 (25.0)	0.58 (0.35, 0.94)*	
Q4 (>137.4)	100 (24.6)	158 (25.0)	0.67 (0.39, 1.14)	

Results: Women with the highest intakes of supplemental selenium (>20 μg/d) had an ~30% lower risk of ovarian cancer than those with no supplemental intake (OR: 0.67; 95% CI: 0.46, 0.97; *P*-trend = 0.035). This inverse association was stronger in current smokers (OR: 0.13; 95% CI: 0.04, 0.46; *P*-trend = 0.001). There was no association with dietary selenium. The associations with carotenoid intakes were weak and nonsignificant (*P* = 0.07–0.60). We observed no association with dietary or supplemental intake of vitamin C or vitamin E. There were no appreciable differences in results between serous and nonserous tumors.

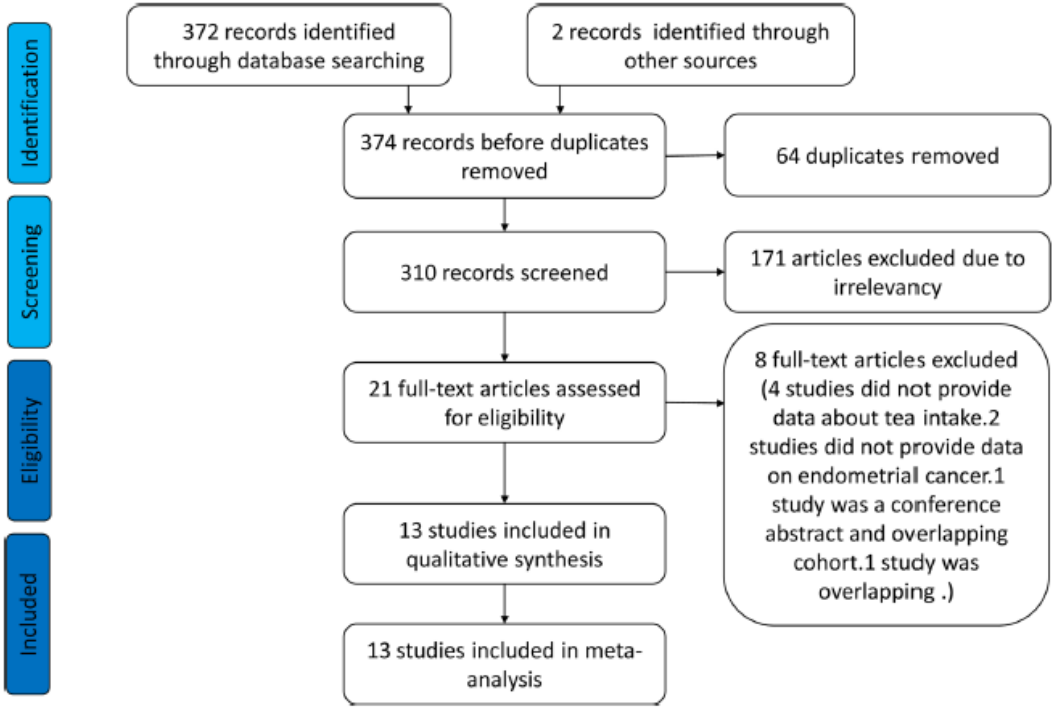
Ernährung und Tumorüberleben

Risikoreduktion für die Ausbildung eines Endometriumkarzinoms durch den regelmäßigen Konsum von grünem Tee

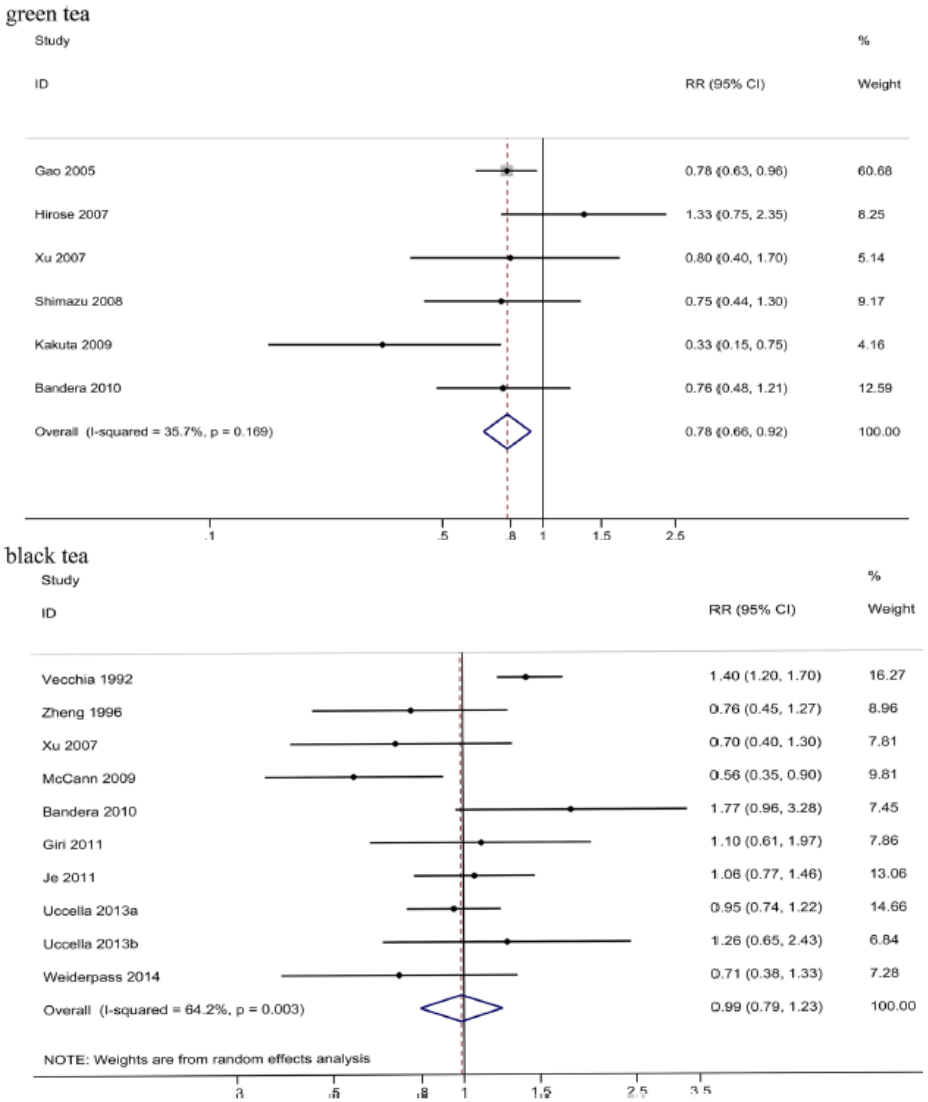
Green tea, black tea consumption and risk of endometrial cancer: a systematic review and meta-analysis

Quan Zhou[1] · Hui Li[2] · Jian-Guo Zhou[3] · Yuan Ma[4] · Tao Wu[2] · Hu Ma[3]

Arch Gynecol Obstet (2016) 293:143–155



Ernährung und Tumorüberleben



Results For green tea, the summary RR indicated that the highest green tea consumption was associated with a reduced risk of EC (RR 0.78, 95 % CI 0.66–0.92). Furthermore, an increase in green tea consumption of one cup per day was associated with an 11 % decreased risk of developing EC. (RR 0.89, 95 % CI 0.84–0.94). For black tea, no statistically significant association was observed in the meta-analysis (highest versus non/lowest, RR 0.99, 95 % CI 0.79–1.23; increment of one cup/day, RR 0.99, 95 % CI 0.94–1.03). The power of the estimate of green tea and black tea with risk of EC was 84.33 and 5.07 %, respectively. The quality of evidence for the association between green and black tea with EC risk was moderate and very low, respectively.

Conclusions The results from this meta-analysis indicate that green tea, but not black tea, may be related to a reduction of EC risk. Large population-based randomized controlled trials and large prospective cohort studies are required to obtain a definitive conclusion and determine the mechanisms underlying this association.

Ernährung und Tumorüberleben

Ernährungsgewohnheiten und ihr Einfluss auf das Gesamtüberleben bei Patientinnen mit Ovarialkarzinomen

DIETARY INFLUENCES ON SURVIVAL AFTER OVARIAN CANCER

Christina M. Nagle[1]*, David M. Purdie[1,2], Penelope M. Webb[1,2], Adèle Green[1,2], Philip W. Harvey[1] and Christopher J. Bain[1]
[1]*School of Population Health, University of Queensland, Brisbane, Australia*

Int. J. Cancer: **106,** 264–269 (2003)

We evaluated the effects of various food groups and micronutrients in the diet on survival among women who originally participated in a population-based case-control study of ovarian cancer conducted across 3 Australian states between 1990 and 1993. This analysis included 609 women with invasive epithelial ovarian cancer, primarily because there was negligible mortality in women with borderline tumors. The women's usual diet was assessed using a validated food frequency questionnaire. Deaths in the cohort were identified using state-based cancer registries and the Australian National Death Index (NDI). Crude 5-year survival probabilities

Ernährung und Tumorüberleben

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[1]*School of Population Health, University of Queensland, Brisbane, Australia*

TABLE II – THE EFFECTS ON VARIOUS FOOD GROUPS AND COMPONENTS ON OVARIAN CANCER SURVIVAL

Daily intake	Total	% Dead	Crude 5-year survival % (SE %)	Adjusted[1] hazard ratio (95% CI)	*p* trend
All vegetables[2]					
<3.9 serves	201	64	44 (4)	1.0	
3.9–5.56 serves	201	63	43 (4)	1.08 (0.82–1.42)	
>5.56 serves	207	58	50 (3)	0.75 (0.57–0.99)	0.01
Cruciferous vegetables[3]					
<0.41 serves	201	65	42 (4)	1.0	
0.41–0.83 serves	203	61	44 (4)	0.87 (0.67–1.13)	
>0.83 serves	205	58	49 (4)	0.75 (0.57–0.98)	0.03
Yellow vegetables[4]					
<0.6 serves	182	62	44 (4)	1.0	
0.6–0.99 serves	196	59	47 (4)	0.96 (0.74–1.25)	
>0.99 serves	231	62	45 (3)	0.98 (0.73–1.31)	0.72
All fruit					
<2.79 serves	202	59	46 (4)	1.0	
2.79–4.49 serves	200	61	45 (4)	0.95 (0.72–1.26)	
>4.49 serves	207	63	44 (3)	0.89 (0.67–1.18)	0.59
Fibre[5]					
Low [18.2g]	188	59	49 (4)	1.0	
Medium [26 g]	213	58	47 (3)	1.02 (0.77–1.34)	
High [35.5 g]	208	67	40 (3)	0.99 (0.75–1.29)	0.99
Carbohydrate					
<192 g	201	65	42 (4)	1.0	
192–263 g	206	58	48 (3)	0.73 (0.53–0.99)	
>263 g	202	60	44 (3)	0.85 (0.57–1.28)	0.48
Vitamin E (from foods)[5]					
Low [7.2 mg]	204	63	44 (4)	1.0	
Medium [10.1 mg]	209	61	44 (4)	0.94 (0.72–1.22)	
High [12.4 mg]	196	60	48 (4)	0.76 (0.58–1.01)	0.04
Vitamin C (from foods)[5]					
Low [108 mg]	195	60	46 (4)	1.0	
Medium [170 mg]	206	61	46 (4)	1.01 (0.77–1.31)	
High [256 mg]	208	50	44 (3)	0.92 (0.71–1.21)	0.65
Beta-carotene					
<4387 µg	201	61	47 (4)	1.0	
4387–6930 µg	201	61	44 (4)	1.09 (0.83–1.43)	
>6930 µg	207	61	45 (3)	1.08 (0.82–1.42)	0.85
Protein					
<74.5 g	205	65	40 (3)	1.0	
74.5–98.5 g	202	60	48 (4)	0.80 (0.60–1.07)	
>98.5 g	202	59	46 (3)	0.72 (0.50–1.04)	0.09
White Meat[6]					
<0.3 serves	202	65	40 (3)	1.0	
0.3–0.54 serves	191	58	48 (4)	0.81 (0.63–1.06)	
>0.54 serves	216	61	47 (3)	0.78 (0.6–1.01)	0.07
Red meat					
<0.5 serves	209	67	40 (3)	1.0	
0.5–0.86 serves	189	58	47 (4)	0.89 (0.68–1.18)	
>0.86 serves	211	58	49 (4)	0.76 (0.58–1.00)	0.06

Ernährung und Tumorüberleben

DIETARY INFLUENCES ON SURVIVAL AFTER OVARIAN CANCER

Christina M. Nagle[1]*, David M. Purdie[1,2], Penelope M. Webb[1,2], Adèle Green[1,2], Philip W. Harvey[1] and Christopher J. Bain[1]
[1]*School of Population Health, University of Queensland, Brisbane, Australia*

were obtained from Cox regression models. After adjusting for important confounding factors, a survival advantage was observed for those who reported higher intake of vegetables in general (HR = 0.75, 95% CI = 0.57–0.99, *p*-value trend 0.01 for the highest third, compared to the lowest third), and cruciferous vegetables in particular (HR = 0.75, 95% CI = 0.57–0.98, *p*-value trend 0.03), and among women in the upper third of intake of vitamin E (HR = 0.76, 95% CI = 0.58–1.01, *p*-value trend 0.04). Inverse associations were also seen with protein (*p*-value trend 0.09), red meat (*p*-value trend 0.06) and white meat (*p*-value trend 0.07), and modest positive trends (maximum 30% excess) with lactose (*p*-value trend 0.04), calcium and dairy products. Although much re-

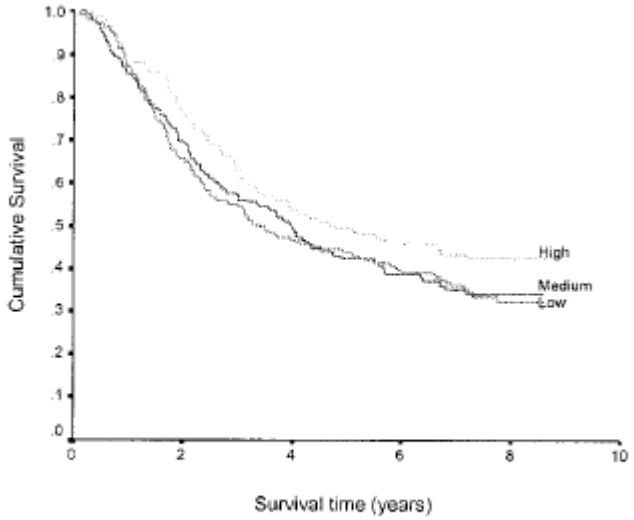


FIGURE 1 – Kaplan-Meier survival curves for vegetable consumption. Low, <3.9 servings/day; Medium, 3.9–5.6 servings/day; High, >5.6 servings/day.

Erhöhung des Gesamtüberlebens beim Ovarialkarzinom möglicherweise durch Gemüseverzehr, insbesondere Kohlarten, sowie Vitamin E Supplementation

Naturstoffe in der medikamentösen Tumortherapie

Curcumin

- **Hauptbestandteil von Curcuma longa – *Gelber Ingwer***
- **Gehört zu den bekanntesten Heilpflanzen in der Gynäkologie**

Naturstoffe in der medikamentösen Tumortherapie

Curcumin

Curcumin suppresses cisplatin resistance development partly via modulating extracellular vesicle-mediated transfer of MEG3 and miR-214 in ovarian cancer

Jing Zhang[1] · Jinyu Liu[2] · Xinyan Xu[1] · Li Li[1]

Cancer Chemother Pharmacol (2017) 79:479–487

Purpose To investigate how curcumin alters the extracellular vesicles' (EVs) capability to ship drug resistance in ovarian cancer.

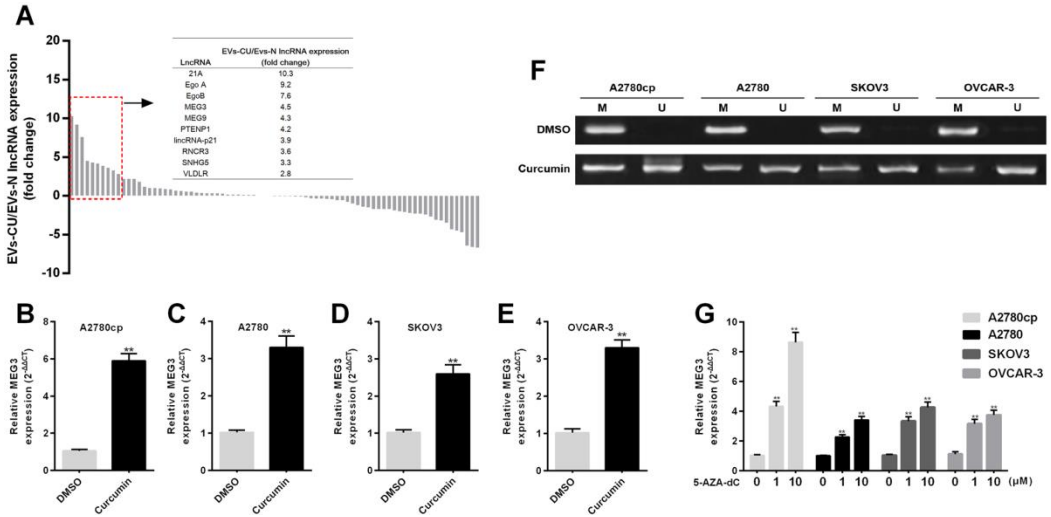
Methods The EVs from cisplatin-resistant A2780cp cells with curcumin treatment (EVs-CU) or without curcumin treatment (EVs-N) were collected for lncRNA profiling. Curcumin's effect on MEG3 promoter methylation and MEG3 expression were studied by MSP and qRT-PCR, respectively. The regulative effect of MEG3 on miR-214 expression and the functional role of EVs mediated transfer of miR-214 in cisplatin resistance were further investigated.

Naturstoffe in der medikamentösen Tumortherapie

Curcumin

Jing Zhang[1] · Jinyu Liu[2] · Xinyan Xu[1] · Li Li[1]

Cancer Chemother Pharmacol (2017) 79:479–487



Results Curcumin weakened the EVs-N's capability to induce drug resistance and induced significant changes of lncRNAs in the EVs. MEG3 is one of the most upregulated lncRNAs. Curcumin led to demethylation in the promoter region of MEG3 and 5-AZA-dC treatment restored MEG3 expression in a dose dependent manner. There were at least two binding sites between MEG3 and miR-214. MEG3 restoration by curcumin significantly reduced miR-214 in cells and in EVs. Functionally, miR-214 inhibition weakened the EVs-N's capability to enhance chemoresistance, while miR-214 overexpression increased the capability of EVs-CU in inducing chemoresistance.

Conclusion

Based on these results, we infer that curcumin can restore lncRNA MEG3 levels in cells and in EVs via acting as a demethylation agent. MEG3 upregulation can decrease EVs mediated transfer of miR-214 in ovarian cancer cells, thereby reducing the development of drug resistance in the recipient cells.

Naturstoffe als Zytostatika

Curcumin

Curcumin promotes the apoptosis of human endometrial carcinoma cells by downregulating the expression of androgen receptor through Wnt signal pathway

W. Feng[1], C.X. Yang[2], L. Zhang[2], Y. Fang[1], M. Yan[2]

Eur. J. Gynaec. Oncol. - ISSN: 0392-2936
XXXV, n. 6, 2014

Objective: The current study aimed to explore the effect of curcumin on androgen receptor (AR) expression in endometrial carcinoma cells, as well as the underlying mechanisms. *Materials and Methods:* Endometrial carcinoma cells were treated with curcumin (10, 50, and 100 μmol/l) for 12, 24, and 48 hours. Their growth curves were drawn using MTT assays and their apoptotic rates were determined using flow cytometry. The mRNA and protein expression of AR was detected using PCR and that of the Wnt signal related nucleoprotein β-cantenin was observed using western blot analysis. The influence of β-cantenin on the action of curcumin was observed. *Results:*

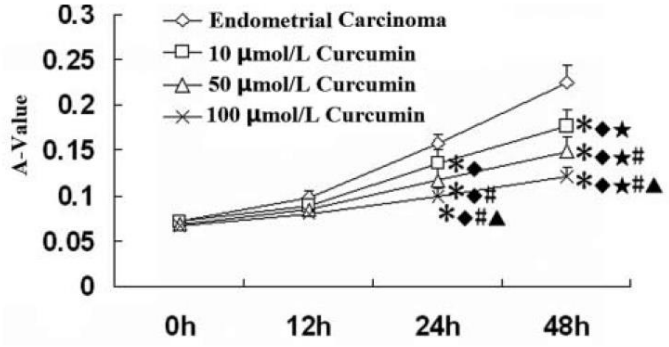


Figure 1. — Effect of curcumin on the proliferation of human endometrial carcinoma cells (X ± S, n = 6).

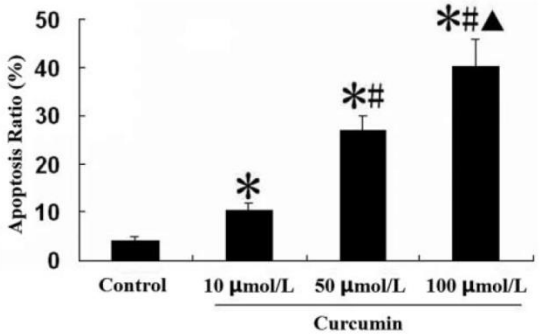
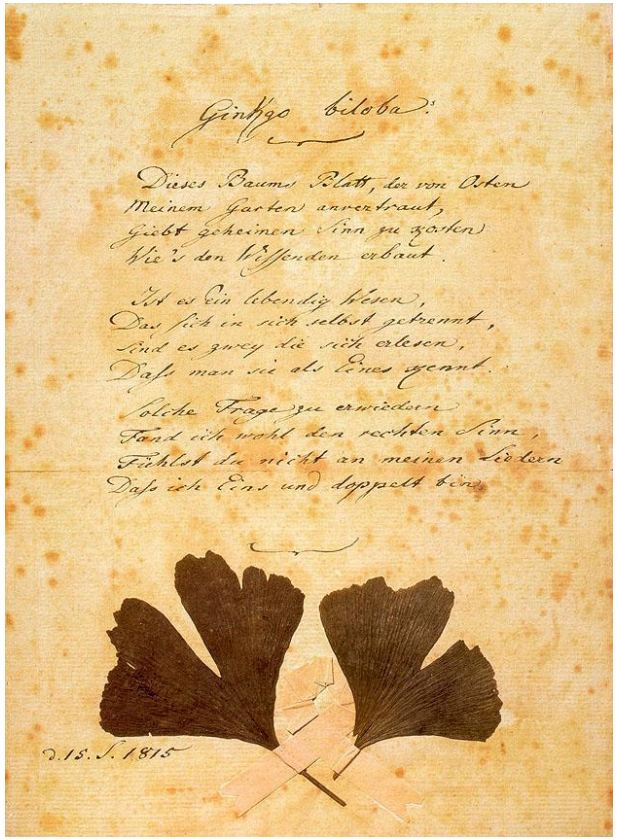


Figure 2. — Effect of curcumin on the apoptosis of human endometrial carcinoma cells (X ± S, n = 6).

Conclusion: Curcumin inhibits the proliferation and apoptosis of human endometrial carcinoma cells by downregulating their AR expression through the Wnt signal pathway.

Naturstoffe in der medikamentösen Tumortherapie

Gingko biloba



Naturstoffe in der medikamentösen Tumortherapie

Gingko biloba

Inhibition of Paclitaxel Metabolism In Vitro in Human Hepatocytes by *Ginkgo biloba* Preparations

Amy S. Etheridge, David J. Kroll & James M. Mathews

To cite this article: Amy S. Etheridge, David J. Kroll & James M. Mathews (2009) Inhibition of Paclitaxel Metabolism In Vitro in Human Hepatocytes by *Ginkgo biloba* Preparations, Journal Of Dietary Supplements, 6:2, 104-110, DOI: 10.1080/19390210902861817

ABSTRACT. Since the late 1980s, chemotherapy-induced cognitive impairment, also known as "chemobrain", has been a recognized side effect in patients undergoing cancer treatment (Matsuda et al., 2005). Although products containing *Ginkgo biloba* may be used by patients undergoing chemotherapy with paclitaxel and other agents, the potential for an herb–drug interaction with this combination has not been adequately explored. This report describes the inhibition of paclitaxel metabolism by *Ginkgo* preparations in vitro in human hepatocytes. Hydrolyzate of *Ginkgo* extract (10–100 mM in terpene lactone concentration) caused a dose-dependent inhibition of the 6α-hydroxylation of paclitaxel, the enzymatic activity responsible for the majority of the clearance of that drug in clinical applications; parent extract had no effect. Contrary to the assumed therapeutic benefit of *Ginkgo*, its concomitant use with

Naturstoffe in der medikamentösen Tumortherapie

Gingko biloba

Inhibition of Paclitaxel Metabolism In Vitro in Human Hepatocytes by *Ginkgo biloba* Preparations

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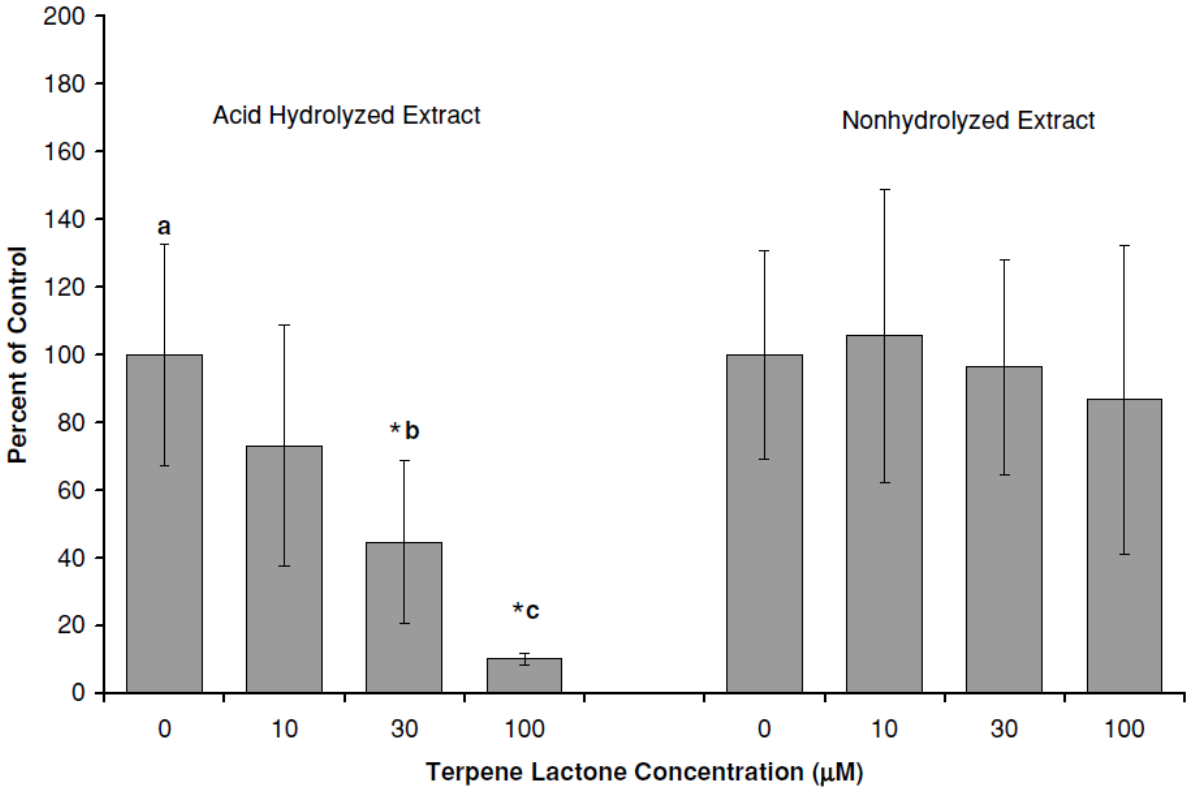


In vivo:

Verzögerte hepatischer Abbau von Paclitaxel bei konkomitanter Gingko Applikation durch Inhibition von CYP2CA durch Gingko

…contrary to the assumed therapeutic benefit of Ginkgo, its concomitant use with paclitaxel could result in elevated blood levels of the chemotherapeutic, with attendant exacerbation of cognitive impairment and other toxic effects

Naturstoffe in der medikamentösen Tumortherapie

Panax ginseng

Erstbeschreibung als Heilpflanze durch Huh Joon 40 v. Christus in Korea

Antioxidanz und Immunmodulator

Caveat: Verlängerte Blutungszeit unter Gingseng Supplementation

1. *Panax ginseng* C. A. Meyer (Korean ginseng)
2. *Panax japonicus* C. A. Meyer (Japanese ginseng)
3. *Panax major* Ting
4. *Panax notoginseng* (Burkill) F. H. Chen (Sanchi ginseng)
5. *Panax omeiensis* J. Wen
6. *Panax pseudoginseng* Wallich
7. *Panax quinquefolius* L. (American ginseng)
8. *Panax sinensis* J. Wen
9. *Panax stipuleanatus* H. T. Tsai & K.M. Feng
10. *Panax trifolius* L. (Dwarf ginseng)
11. *Panax wangianus* Sun
12. *Panx zingiberensis* C.Y. Wu & K.M. Feng
13. *Panax vietnamensis* Ha et Grushv. (Vietnamese ginseng)

Naturstoffe in der medikamentösen Tumortherapie

Panax ginseng

Effect of Red Ginseng on Genotoxicity and Health-Related Quality of Life after Adjuvant Chemotherapy in Patients with Epithelial Ovarian Cancer: A Randomized, Double Blind, Placebo-Controlled Trial

Hee Seung Kim [1], Mi-Kyung Kim [2], Maria Lee [1], Byung-Su Kwon [3], Dong Hoon Suh [4] and Yong Sang Song [1,5,*]

[1] Department of Obstetrics and Gynecology, Seoul National University College of Medicine, Seoul 03080, Korea; bboddi0311@gmail.com (H.S.K.); marialeemd@gmail.com (M.L.)

Nutrients **2017**, *9*, 772

Abstract: We evaluated the effect of red ginseng on toxicity, health-related quality of life (HRQL) and survival after adjuvant chemotherapy in patients with epithelial ovarian cancer (EOC). A total of 30 patients with EOC were randomly assigned to placebo (n = 15) and red ginseng groups (n = 15). All patients took placebo or red ginseng (3000 mg/day) for three months. Then, we compared changes of genotoxicity, HRQL and survival between the two groups. As a result, red ginseng

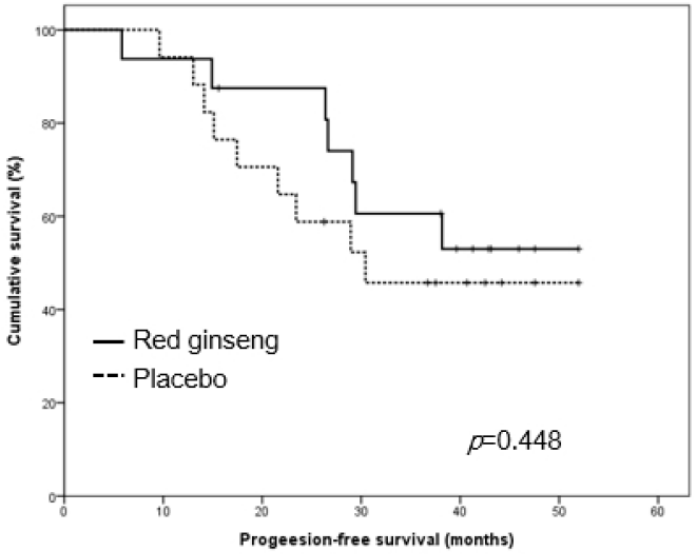
Naturstoffe in der medikamentösen Tumortherapie

Panax ginseng

Nutrients **2017**, *9*, 772

Table 4. Evaluation of the effect of red ginseng on health-related quality of life.

Outcomes	Placebo (n = 15)		p Value	Red Ginseng (n = 15)		p Value
	Week 0	Week 12		Week 0	Week 12	
European Organization for Research and Treatment of Cancer Quality of Life (EORTC QLQ)-C30						
Functional scale						
Emotional	37.5 ± 10.9	38.7 ± 13.9	0.702	44.9 ± 15.3	37.5 ± 12.7	0.027
Symptom scale						
Fatigue	53.7 ± 11.8	45.8 ± 13.9	0.131	58.8 ± 19.2	46.1 ± 16.2	0.012
Nausea and vomiting	30.5 ± 6.4	27.3 ± 5.0	0.157	37.5 ± 15.3	27.2 ± 6.6	0.004
Dyspnea	40.6 ± 22.1	31.3 ± 14.4	0.161	47.1 ± 17.4	35.3 ± 17.8	0.021
Brief Fatigue Inventory (BFI)						
Severity						
Worst fatigue	4.25 ± 2.27	3.62 ± 2.71	0.658	5.59 ± 3.20	4.00 ± 3.32	0.026
Interference	19.25 ± 10.33	11.38 ± 11.84	0.084	23.24 ± 17.79	14.29 ± 17.59	0.014
Brief Pain Inventory (BPI)						
Pain interference						
Enjoyment of life	3.0 ± 3.6	1.8 ± 3.0	0.138	1.8 ±. 2.3	0.4 ± 0.7	0.035
Hospital Anxiety and Depression Scale (HADS)						
Anxiety	7.8 ± 2.4	8.4 ± 1.5	0.119	9.1 ± 2.6	8.0 ± 2.6	0.015
Sleep Scale from the Medical Outcome Study (MOS-SS)						
Daytime somnolence	74.5 ± 14.8	77.5 ± 16.8	0.342	74.7 ± 17.1	83.0 ± 8.9	0.043



The current study shows that red ginseng may be effective to reduce genotoxicity and improve HRQL in patients with EOC who received chemotherapy after surgery. Moreover, red ginseng can be taken safely, but it has no effect on improved survival of EOC. However, the current study has a limitations of the small sample size, which can be estimated from a few studies where genotoxicity was investigated. Thus, the results from the current study should be proven in large-scale trials in the future.

Universitätsklinikum Leipzig
Medizin ist unsere Berufung.

Vielen Dank für Ihre Aufmerksamkeit!