Wissenschaftliche Publikationen aus dem Institut für Ernährungswissenschaften veröffentlicht von Juni bis Oktober 2021

Direct and Base Excision Repair-Mediated Regulation of a GC-Rich *cis*-Element in Response to 5-Formylcytosine and 5-Carboxycytosine

Müller N, Ponkkonen E, Carell T, Khobta A
Int. J. Mol. Sci. 2021, 22, 11025. https://doi.org/10.3390/ijms222011025

Stepwise oxidation of the epigenetic mark 5-methylcytosine and base excision repair (BER) of the resulting 5-formylcytosine (5-fC) and 5-carboxycytosine (5-caC) may provide a mechanism for reactivation of epigenetically silenced genes; however, the functions of 5-fC and 5-caC at defined gene elements are scarcely explored. We analyzed the expression of reporter constructs containing either 2′-deoxy-(5-fC/5-caC) or their BER-resistant 2′-fluorinated analogs, asymmetrically incorporated into CG-dinucleotide of the GC box cis-element (5′-TGGGCGGAGC) upstream from the RNA polymerase II core promoter. In the absence of BER, 5-caC caused a strong inhibition of the promoter activity, whereas 5-fC had almost no effect, similar to 5-methylcytosine or 5-hydroxymethylcytosine. BER of 5-caC caused a transient but significant promoter reactivation, succeeded by silencing during the following hours. Both responses strictly required thymine DNA glycosylase (TDG); however, the silencing phase additionally demanded a 5′-endonuclease (likely APE1) activity and was also induced by 5-fC or an apurinic/apyrimidinic site. We propose that 5-caC may act as a repressory mark to prevent premature activation of promoters undergoing the final stages of DNA demethylation, when the symmetric CpG methylation has already been lost. Remarkably, the downstream promoter activation or repression responses are regulated by two separate BER steps, where TDG and APE1 act as potential switches.

Pflanzenöle und -fette
Inhaltsstoffe und gesundheitliche Wirkungen

Glei M
ERNÄHRUNGSUMSCHAU, Sonderheft 6, 2021, S. 56-66
Als essenzielle Bestandteile biologischer Membranen und wichtige Energiereserve kommen Fette in fast allen Lebensmitteln natürlicherweise vor. Wesentliche Lieferanten sind neben Fleisch, Milch und daraus hergestellten Produkten vor allem Pflanzenöle. Den Nahrungsfetten kommt aufgrund des im Vergleich zu den anderen energieliefernden Nahrungsbestandteilen hohen Energiegehalts von 9 kcal/g bzw. 37 kJ/g eine besondere Bedeutung in der Ernährung zu. Darüber hinaus ist das Fett Träger fettlöslicher Vitamine sowie von Aroma- und Geschmacksstoffen. Fett wirkt sich günstig auf die Textur von Lebensmitteln aus und verfügt über ein hohes Sättigungspotenzial. Der Artikel stellt die wichtigsten Pflanzenöle und -fette und ihre Bedeutung für die Ernährung vor.

Fermentation profile, cholesterol-reducing properties and chemopreventive potential of β-glucans from *Levilactobacillus brevis* and *Pediococcus claussenii* - a comparative study with β-glucans from different sources.

Schlörmann W, Bockwoldt JA, Mayr MF, Lorkowski S, Dawczynski C, Rohn S, Ehrmann MA, Glei M.
Food & Function, 2021, **12**, 10615 – 10631. doi: 10.1039/d1fo02175c.

The aim of the present study was to investigate whether β-glucans obtained from the lactic acid bacteria (LAB) *Levilactobacillus (L.) brevis* and *Pediococcus (P.) claussenii* exhibit similar physiological effects such as cholesterol-binding capacity (CBC) as the structurally different β-glucans from oat, barley, and yeast as well as curdlan. After *in vitro* fermentation, fermentation supernatants (FSs) and/or -pellets (FPs) were analyzed regarding the concentrations of short-chain fatty acids (SCFAs), ammonia, bile acids, the relative abundance of bacterial taxa and chemopreventive effects (growth inhibition, apoptosis, genotoxicity) in LT97 colon adenoma cells. Compared to other glucans, the highest CBC was determined for oat β-glucan (65.9 ± 8.8 mg g^{-1}, $p < 0.05$). Concentrations of SCFA were increased in FSs of all β-glucans (up to 2.7-fold). The lowest concentrations of ammonia (down to 0.8 ± 0.3 mmol L^{-1}) and bile acids (2.5-5.2 µg mL^{-1}) were detected in FSs of the β-glucans from oat, barley, yeast, and curdlan. The various β-glucans differentially modulated the relative abundance of bacteria families and reduced the Firmicutes/Bacteroidetes ratio. Treatment of LT97 cells with the FSs led to a significant dose-dependent growth reduction and increase in caspase-3 activity without exhibiting genotoxic effects. Though the different β-glucans show different fermentation profiles as well as cholesterol- and bile acid-reducing properties, they exhibit comparable chemopreventive effects.

Metformin alters therapeutic effects in the BALB/c tumor therapy model

Meyer FB, Goebel S, Spangel SB, Leovsky C, Hoelzer D, Thierbach R
BMC Cancer. 2021; 21(1):629. doi: 10.1186/s12885-021-08354-x.

Background: Despite considerable medical proceedings, cancer is still a leading cause of death. Major problems for tumor therapy are chemoresistance as well as toxic side effects. In recent years, the additional treatment with the antidiabetic drug metformin during chemotherapy showed promising results in some cases. The aim of this study was to develop an in vitro tumor therapy model in order to further investigate the potential of a combined chemotherapy with metformin.
Methods: Cytotoxic effects of a combined treatment on BALB/c fibroblasts were proven by the resazurin assay. Based on the BALB/c cell transformation assay, the BALB/c tumor therapy model was established successfully with four different and widely used chemotherapeutics from different categories. Namely, Doxorubicin as a type-II isomerase inhibitor, Docetaxel as a spindle toxin, Mitomycin C as an alkylating agent and 5-Fluorouracil as an antimetabolite. Moreover, glucose consumption in the medium supernatant was measured and protein expressions were determined by Western Blotting.
Results: Initial tests for the combined treatment with metformin indicated unexpected results as metformin could partly mitigate the cytotoxic effects of the chemotherapeutic agents. These results were further confirmed as metformin induced resistance to some of the drugs when applied simultaneously in the tumor therapy model. Mechanistically, an increased glucose consumption was observed in non-transformed cells as well as in the mixed population of malignant transformed cell foci and non-transformed monolayer cells, suggesting that metformin could also increase glucose consumption in transformed cells.
Conclusion: In conclusion, this study suggests a cautious use of metformin during chemotherapy. Moreover, the BALB/c tumor therapy model offers a potent tool for further mechanistic studies of drug-drug interactions during cancer therapy.

The Nutritional Supply of Iodine and Selenium Affects Thyroid Hormone Axis Related Endpoints in Mice

Lossow K, Renko K, Schwarz M, Schomburg L, Schwerdtle T, Kipp AP
Nutrients 2021 Oct DOI: 10.3390/nu13113773

Selenium and iodine are the two central trace elements for the homeostasis of thyroid hormones but additional trace elements such as iron, zinc, and copper are also involved. To compare the primary effects of inadequate intake of selenium and iodine on the thyroid gland, as well as the target organs of thyroid hormones such as liver and kidney, mice were subjected to an eight-week dietary intervention with low versus adequate selenium and iodine supply. Analysis of trace element levels in serum, liver, and kidney demonstrated a successful intervention. Markers of the selenium status were unaffected by the iodine supply. The thyroid gland was able to maintain serum thyroxine levels even under selenium-deficient conditions, despite reduced selenoprotein expression in liver and kidney, including deiodinase type 1. Thyroid hormone target genes responded to the altered selenium and iodine supply, whereas the iron, zinc, and copper homeostasis remained unaffected. There was a notable interaction between thyroid hormones and copper, which requires further clarification. Overall, the effects of an altered selenium and iodine supply were pronounced in thyroid hormone target tissues, but not in the thyroid gland.

Ageing-associated effects of a long-term dietary modulation of four trace elements in mice

Wandt VK, Winkelbeiner N, Lossow K, Kopp JF, Schwarz M, Alker W, Nicolai MM, Simon L, Dietzel C, Hertel B, Pohl G, Ebert F, Schomburg L, Bornhorst J, Haase H, Kipp AP, Schwerdtle T
Redox Biol. 2021 Oct;46:102083. doi: 10.1016/j.redox.2021.102083. Epub 2021 Jul 27.

Trace elements (TEs) are essential for diverse processes maintaining body function and health status. The complex regulation of the TE homeostasis depends among others on age, sex, and nutritional status. If the TE homeostasis is disturbed, negative health consequences can result, e.g., caused by impaired redox homeostasis and genome stability maintenance. Based on age-related shifts in TEs which have been described in mice well-supplied with TEs, we aimed to understand effects of a long-term feeding with adequate or suboptimal amounts of four TEs in parallel. As an additional intervention, we studied mice which received an age-adapted diet with higher concentrations of selenium and zinc to counteract the age-related decline of both TEs. We conducted comprehensive analysis of diverse endpoints indicative for the TE and redox status, complemented by analysis of DNA (hydroxy)methylation and markers denoting genomic stability maintenance. TE concentrations showed age-specific alterations which were relatively stable and independent of their nutritional supply. In addition, hepatic DNA hydroxymethylation was significantly increased in the elderly mice and markers indicative for the redox status were modulated. The reduced nutritional supply with TEs inconsistently affected their status, with most severe effects regarding Fe deficiency. This may have contributed to the sex-specific differences observed in the alterations related to the redox status and DNA repair activity. Overall, our results highlight the complexity of factors impacting on the TE status and its physiological consequences. Alterations in TE supply, age, and sex proved to be important determinants that need to be taken into account when considering TE interventions for improving general health and supporting convalescence in the clinics.

The Trace Element Selenium Is Important for Redox Signaling in Phorbol Ester-Differentiated THP-1 Macrophages

Theresa Wolfram, Leonie M. Weidenbach, Johanna Adolf, Maria Schwarz, Patrick Schädel, André Gollowitzer, Oliver Werz, Andreas Koeberle, Anna P. Kipp, Solveigh Koeberle
International Journal of Molecular Sciences, October 2021, 22(20):11060
DOI: 10.3390/ijms222011060

Physiological selenium (Se) levels counteract excessive inflammation, with selenoproteins shap-ing the immunoregulatory cytokine and lipid mediator profile. How exactly differentiation of monocytes into macrophages influences the expression of the selenoproteome in concert with the Se supply remains obscure. THP-1 monocytes were differentiated with phorbol 12-myristate 13-acetate (PMA) into macrophages and (i) the expression of selenoproteins, (ii) differentiation markers, (iii) the activity of NF-κB and NRF2, as well as (iv) lipid mediator profiles were analyzed. Se and differentiation affected the expression of selenoproteins in a heterogeneous manner. GPX4 expression was substantially decreased during differentiation, whereas GPX1 was not affected. Moreover, Se increased the expression of selenoproteins H and F, which was further enhanced by differentiation for selenoprotein F and diminished for selenoprotein H. Notably, LPS-induced expression of NF-κB target genes was facilitated by Se, as was the release of COX- and LOX-derived lipid mediators and substrates required for lipid mediator biosynthesis. This in-cluded TBX2, TBX3, 15-HETE, and 12-HEPE, as well as arachidonic acid (AA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA). Our results indicate that Se enables macrophages to accurately adjust redox-dependent signaling and thereby modulate downstream lipid mediator profiles.

Production and purification of homogenous recombinant human selenoproteins reveals a unique codon skipping event in E. coli and GPX4-specific affinity to bromosulfophthalein

Cheng Q, Roveri A, Cozza G, Bordin L, Rohn I, Schwerdtle T, Kipp A, Ursini F, Maiorino M, Miotto G, Arnér ESJ
Redox Biol. 2021 Oct;46:102070. doi: 10.1016/j.redox.2021.102070. Epub 2021 Jul 17.

Selenoproteins are translated via animal domain-specific elongation machineries that redefine dedicated UGA opal codons from termination of translation to selenocysteine (Sec) insertion, utilizing specific tRNA species and Sec-specific elongation factors. This has made recombinant production of mammalian selenoproteins in E. coli technically challenging but recently we developed a methodology that enables such production, using recoding of UAG for Sec in an RF1-deficient host strain. Here we used that approach for production of the human glutathione peroxidases 1, 2 and 4 (GPX1, GPX2 and GPX4), with all these three enzymes being important antioxidant selenoproteins. Among these, GPX4 is the sole embryonically essential enzyme, and is also known to be essential for spermatogenesis as well as protection from cell death through ferroptosis. Enzyme kinetics, ICP-MS and mass spectrometry analyses of the purified recombinant proteins were used to characterize selenoprotein characteristics and their Sec contents. This revealed a unique phenomenon of one-codon skipping, resulting in a lack of a single amino acid at the position corresponding to the selenocysteine (Sec) residue, in about 30% of the recombinant GPX isoenzyme products. We furthermore confirmed the previously described UAG suppression with Lys or Gln as well as a minor suppression with Tyr, together resulting in about 20% Sec contents in the full-length proteins. No additional frameshifts or translational errors were detected. We subsequently found that Sec-containing GPX4 could be further purified over a bromosulfophthalein-column, yielding purified recombinant GPX4 with close to complete Sec contents. This production method for homogenously purified GPX4 should help to further advance the studies of this important selenoprotein.

Endogenous vitamin E metabolites mediate allosteric PPARγ activation with unprecedented co-regulatory interactions

Willems S, Gellrich L, Chaikuad A, Kluge S, Werz O, Heering J, Knapp S, Lorkowski S, Schubert-Zsilavecz M, Merk D
Cell Chem Biol 2021; in press. DOI: 10.1016/j.chembiol.2021.04.019.

Vitamin E exhibits pharmacological effects beyond established antioxidant activity suggesting involvement of unidentified mechanisms. Here, we characterize endogenously formed tocopherol carboxylates and the vitamin E mimetic garcinoic acid (GA) as activators of the peroxisome proliferator-activated receptor gamma (PPARγ). Co-stimulation of PPARγ with GA and the orthosteric agonist pioglitazone resulted in additive transcriptional activity. In line with this, the PPARγ-GA complex adopted a fully active conformation and interestingly contained two bound GA molecules with one at an allosteric site. A co-regulator interaction scan demonstrated an unanticipated co-factor recruitment profile for GA-bound PPARγ compared with canonical PPARγ agonists and gene expression analysis revealed different effects of GA and pioglitazone on PPAR signaling in hepatocytes. These observations reveal allosteric mechanisms of PPARγ modulation as an alternative avenue to PPARγ targeting and suggest contributions of PPARγ activation by α-13-tocopherolcarboxylate to the pharmacological effects of vitamin E.

The burden of dementia due to Down syndrome, Parkinson's disease, stroke, and traumatic brain injury: a systematic analysis for the Global Burden of Disease Study 2019

GBD 2019 Dementia Collaborators
Neuroepidemiology 2021; 55(4):286-296. DOI: 10.1159/000515393

Background: In light of the increasing trend in the global number of individuals affected by dementia and the lack of any available disease-modifying therapies, it is necessary to fully understand and quantify the global burden of dementia. This work aimed to estimate the proportion of dementia due to Down syndrome, Parkinson's disease, clinical stroke, and traumatic brain injury (TBI), globally and by world region, in order to better understand the contribution of clinical diseases to dementia prevalence.

Methods: Through literature review, we obtained data on the relative risk of dementia with each condition and estimated relative risks by age using a Bayesian meta-regression tool. We then calculated population attributable fractions (PAFs), or the proportion of dementia attributable to each condition, using the estimates of relative risk and prevalence estimates for each condition from the Global Burden of Disease Study 2019. Finally, we multiplied these estimates by dementia prevalence to calculate the number of dementia cases attributable to each condition.

Findings: For each clinical condition, the relative risk of dementia decreased with age. Relative risks were highest for Down syndrome, followed by Parkinson's disease, stroke, and TBI. However, due to the high prevalence of stroke, the PAF for dementia due to stroke was highest. Together, Down syndrome, Parkinson's disease, stroke, and TBI explained 10.0% (95% UI: 6.0-16.5) of the global prevalence of dementia.

Interpretation: Ten percent of dementia prevalence globally could be explained by Down syndrome, Parkinson's disease, stroke, and TBI. The quantification of the proportion of dementia attributable to these 4 conditions constitutes a small contribution to our overall understanding of what causes dementia. However, epidemiological research into modifiable risk factors as well as basic science research focused on elucidating intervention approaches to prevent or delay the neuropathological changes that commonly characterize dementia will be critically important in future efforts to prevent and treat disease.

Global, regional, and national burden of stroke and its risk factors, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019

GBD 2019 Stroke Collaborators
Lancet Neurology 2021; 20(10):795-820. DOI: 10.1016/S1474-4422(21)00252-0

Background: Regularly updated data on stroke and its pathological types, including data on their incidence, prevalence, mortality, disability, risk factors, and epidemiological trends, are important for evidence-based stroke care planning and resource allocation. The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) aims to provide a standardised and comprehensive measurement of these metrics at global, regional, and national levels.

Methods: We applied GBD 2019 analytical tools to calculate stroke incidence, prevalence, mortality, disability-adjusted life-years (DALYs), and the population attributable fraction (PAF) of DALYs (with corresponding 95% uncertainty intervals [UIs]) associated with 19 risk factors, for 204 countries and territories from 1990 to 2019. These estimates were provided for ischaemic stroke, intracerebral haemorrhage, subarachnoid haemorrhage, and all strokes combined, and stratified by sex, age group, and World Bank country income level.

Findings: In 2019, there were 12·2 million (95% UI 11·0-13·6) incident cases of stroke, 101 million (93·2-111) prevalent cases of stroke, 143 million (133-153) DALYs due to stroke, and 6·55 million (6·00-7·02) deaths from stroke. Globally, stroke remained the second-leading cause of death (11·6% [10·8-12·2] of total deaths) and the third-leading cause of death and disability combined (5·7% [5·1-6·2] of total DALYs) in 2019. From 1990 to 2019, the absolute number of incident strokes increased by 70·0% (67·0-73·0), prevalent strokes increased by 85·0% (83·0-88·0), deaths from stroke increased by 43·0% (31·0-55·0), and DALYs due to stroke increased by 32·0% (22·0-42·0). During the same period, age-standardised rates of stroke incidence decreased by 17·0% (15·0-18·0), mortality decreased by 36·0% (31·0-42·0), prevalence decreased by 6·0% (5·0-7·0), and DALYs decreased by 36·0% (31·0-42·0). However, among people younger than 70 years, prevalence rates increased by 22·0% (21·0-24·0) and incidence rates increased by 15·0% (12·0-18·0). In 2019, the age-standardised stroke-related mortality rate was 3·6 (3·5-3·8) times higher in the World Bank low-income group than in the World Bank high-income group, and the age-standardised stroke-related DALY rate was 3·7 (3·5-3·9) times higher in the low-income group than the high-income group. Ischaemic stroke constituted 62·4% of all incident strokes in 2019 (7·63 million [6·57-8·96]), while intracerebral haemorrhage constituted 27·9% (3·41 million [2·97-3·91]) and subarachnoid haemorrhage constituted 9·7% (1·18 million [1·01-1·39]). In 2019, the five leading risk factors for stroke were high systolic blood pressure (contributing to 79·6 million [67·7-90·8] DALYs or 55·5% [48·2-62·0] of total stroke DALYs), high body-mass index (34·9 million [22·3-48·6] DALYs or 24·3% [15·7-33·2]), high fasting plasma glucose (28·9 million [19·8-41·5] DALYs or 20·2% [13·8-29·1]), ambient particulate matter pollution (28·7 million [23·4-33·4] DALYs or 20·1% [16·6-23·0]), and smoking (25·3 million [22·6-28·2] DALYs or 17·6% [16·4-19·0]).

Interpretation: The annual number of strokes and deaths due to stroke increased substantially from 1990 to 2019, despite substantial reductions in age-standardised rates, particularly among people older than 70 years. The highest age-standardised stroke-related mortality and DALY rates were in the World Bank low-income group. The fastest-growing risk factor for stroke between 1990 and 2019 was high body-mass index. Without urgent implementation of effective primary prevention strategies, the stroke burden will probably continue to grow across the world, particularly in low-income countries.

Spatial, temporal, and demographic patterns in prevalence of smoking tobacco use and attributable disease burden in 204 countries and territories, 1990-2019: a systematic analysis from the Global Burden of Disease Study 2019

GBD 2019 Tobacco Collaborators
Lancet 2021; 397(10292):2337-2360. DOI: 10.1016/S0140-6736(21)01169-7

Background: Ending the global tobacco epidemic is a defining challenge in global health. Timely and comprehensive estimates of the prevalence of smoking tobacco use and attributable disease burden are needed to guide tobacco control efforts nationally and globally.

Methods: We estimated the prevalence of smoking tobacco use and attributable disease burden for 204 countries and territories, by age and sex, from 1990 to 2019 as part of the Global Burden of Diseases, Injuries, and Risk Factors Study. We modelled multiple smoking-related indicators from 3625 nationally representative surveys. We completed systematic reviews and did Bayesian meta-regressions for 36 causally linked health outcomes to estimate non-linear dose-response risk curves for current and former smokers. We used a direct estimation approach to estimate attributable burden, providing more comprehensive estimates of the health effects of smoking than previously available.

Findings: Globally in 2019, 1·14 billion (95% uncertainty interval 1·13-1·16) individuals were current smokers, who consumed 7·41 trillion (7·11-7·74) cigarette-equivalents of tobacco in 2019. Although prevalence of smoking had decreased significantly since 1990 among both males (27·5% [26·5-28·5] reduction) and females (37·7% [35·4-39·9] reduction) aged 15 years and older, population growth has led to a significant increase in the total number of smokers from 0·99 billion (0·98-1·00) in 1990. Globally in 2019, smoking tobacco use accounted for 7·69 million (7·16-8·20) deaths and 200 million (185-214) disability-adjusted life-years, and was the leading risk factor for death among males (20·2% [19·3-21·1] of male deaths). 6·68 million [86·9%] of 7·69 million deaths attributable to smoking tobacco use were among current smokers.

Interpretation: In the absence of intervention, the annual toll of 7·69 million deaths and 200 million disability-adjusted life-years attributable to smoking will increase over the coming decades. Substantial progress in reducing the prevalence of smoking tobacco use has been observed in countries from all regions and at all stages of development, but a large implementation gap remains for tobacco control. Countries have a clear and urgent opportunity to pass strong, evidence-based policies to accelerate reductions in the prevalence of smoking and reap massive health benefits for their citizens.

Ernährung bei arterieller Hypertonie

Schumacher S, Dawczynski C, Lorkowski S
Ärzteblatt Thüringen 2021; 32(6):28-29.

Fette auf der Anklagebank

Lorkowski S
UGBforum 2021; 3:138-141.

Unter Ernährungsfachkräften hat sich Unsicherheit breit gemacht. Die Empfehlungen zur Fettzufuhr seien überholt und entsprächen nicht dem aktuellen Stand der Forschung. Ernährungswissenschaftler Professor Stefan Lorkowski hat sich als Anwalt der Fette auf die Suche nach gesicherten Erkenntnissen begeben.

Alcohol consumption and mortality: The Ludwigshafen Risk and Cardiovascular Health (LURIC) study

Moissl AP, Delgado GE, Krämer BK, Dawczynski C, Stojakovic T, März W, Kleber ME, Lorkowski S
Atherosclerosis 2021; 335:119-125. DOI: 10.1016/j.atherosclerosis.2021.08.014

Background and aims: One of the most important risk factors for morbidity and mortality is the consumption of alcohol. The aim of our study was to examine the effect of alcohol consumption on all-cause mortality and cardiovascular mortality.

Methods: The Ludwigshafen Risk and Cardiovascular Health (LURIC) study includes 3316 patients hospitalized for coronary angiography at a tertiary care centre in Southwest Germany. Patients were followed-up for a median of 9.9 (range 0.1-11.9 years) years. Total mortality number in the follow-up period was 995, and the number of incident cases, i.e. cardiovascular death, was 622. Information on alcohol consumption assessed by self-report questionnaires was used to calculate intake in grams of ethanol per day. Associations of alcohol consumption with morbidity and mortality were analysed using Cox proportional hazards regression.

Results: We found significantly increased mortality for patients in the highest alcohol intake group age- and sex-adjusted (hazard ratio of 1.59 (95%CI, 0.93-2.72)) and a reduced risk for the group of low-volume drinkers (hazard ratio of 0.75 (95%CI, 0.65-0.86)). After adjustment for cardiovascular risk factors, the risk difference between abstainers and low-volume drinkers was not significant anymore.

Conclusions: In the LURIC study, the risk of overall mortality and cardiovascular mortality is significantly increased in study participants with very high alcohol consumption and slightly increased in total abstainers as compared to participants with low consumption in unadjusted analysis, replicating the well-known J-curve. Adjusting for cardiovascular risk factors rendered the risk decrease observed for low-volume drinkers insignificant. Therefore, our results do not show a significant health benefit of low-volume alcohol consumption in a cohort of patients at medium-to-high cardiovascular risk.

Exploration of long-chain vitamin E metabolites for the discovery of a highly potent, orally effective, and metabolically stable 5-LOX inhibitor that limits inflammation

Neukirch K, Alsabil K, Dinh CP, Bilancia R, Raasch M, Ville A, Cerqua I, Viault G, Bréard D, Pace S, Temml V, Brunner E, Jordan PM, Marques MC, Loeser K, Gollowitzer A, Permann S, Gerstmeier J, Lorkowski S, Stuppner H, Garscha U, Rodrigues T, Bernardes GJL, Schuster D, Séraphin D, Richomme P, Rossi A, Mosig AS, Roviezzo F, Werz O, Helesbeux JJ, Koeberle A
J Med Chem 2021; 64(15):11496-11526. DOI: 10.1021/acs.jmedchem.1c00806