Selenium and Cancer

https://pubmed.ncbi.nlm.nih.gov/29376219/
Selenium for preventing cancer. 2018
Authors' conclusions: Well-designed and well-conducted RCTs have shown no beneficial effect of selenium supplements in reducing cancer risk (high certainty of evidence). Some RCTs have raised concerns by reporting a higher incidence of high-grade prostate cancer and type 2 diabetes in participants with selenium supplementation. No clear evidence of an influence of baseline participant selenium status on outcomes has emerged in these studies.Observational longitudinal studies have shown an inverse association between selenium exposure and risk of some cancer types, but null and direct relations have also been reported, and no systematic pattern suggesting dose-response relations has emerged. These studies suffer from limitations inherent to the observational design, including exposure misclassification and unmeasured confounding.Overall, there is no evidence to suggest that increasing selenium intake through diet or supplementation prevents cancer in humans. However, more research is needed to assess whether selenium may modify the risk of cancer in individuals with a specific genetic background or nutritional status, and to investigate possible differential effects of various forms of selenium.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8879146/
Potential Role of Selenium in the Treatment of Cancer and Viral Infections. 2022
Selenium has been extensively evaluated clinically as a chemopreventive agent with variable results depending on the type and dose of selenium used. Selenium species are now being therapeutically evaluated as modulators of drug responses rather than as directly cytotoxic agents. In addition, recent data suggest an association between selenium base-line levels in blood and survival of patients with COVID-19. The major focus of this mini review was to summarize: the pathways of selenium metabolism; the results of selenium-based chemopreventive clinical trials; the potential for using selenium metabolites as therapeutic modulators of drug responses in cancer (clear-cell renal-cell carcinoma (ccRCC) in particular); and selenium usage alone or in combination with vaccines in the treatment of patients with COVID-19. Critical therapeutic targets and the potential role of different selenium species, doses, and schedules are discussed.
A study conducted in 18 human subjects treated with 200 µg selenium-enriched broccoli daily for three days showed that selenium supplementation resulted in substantially higher levels of both Th1 and Th2 cytokines secreted by peripheral blood mononuclear cells.
The chemopreventive, cancer-promoting, and anti-cancer effects of selenium are three different aspects of selenium's complicated relationship with cancer. Selenium was prohibited as a food additive by the US FDA for fear of its potential link to cancer as deduced from laboratory animal experiments [17]. However, subsequent studies in 1957 by Klaus Schwartz and Calvin Foltz demonstrated the beneficial effect of selenium intake for humans and mammals by showing that dietary selenium intake protects rats from liver necrosis [1,18]. Selenium was first suggested as a chemopreventive agent in the late 1960s [19] and in the 1990s it was considered a promising cancer preventing agent against different cancer types; however, subsequent clinical trials revealed that selenium did not have chemopreventive properties [20].
Several studies have shown that selenium has a tumor-promoting effect. The NPC trial, for example, found that selenium supplementation (as selenized yeast; 200 µg/day) significantly increased the risk of non-melanoma skin cancer and squamous-cell carcinoma [24]. Another study was conducted on the population of the Reggio Emilia municipality in Italy, who were exposed to 7–9 µg/liter of selenate in tap water from 1975 to 1985. Melanoma incidence was 3.9 times higher in selenium-exposed people than in non-selenium exposed people, according to the findings of this study [25].
Selenium also helps with DNA repair in response to DNA-damaging agents, which improves the effectiveness of chemotherapeutic agents by protecting normal cells from their toxicity.
Selenium was shown to reduce drug detoxification and increase cytotoxic effects of anti-cancer drugs in tumor cells through suppression of the Nrf2/Prx1 pathway, while increasing drug detoxification and decreasing cytotoxicity of anti-cancer drugs toward normal tissues by maintaining redox homeostasis. These opposing effects of selenium depend on cell status.
Selenium is an essential trace element obtained from diet. Deficiency in blood selenium concentrations has been associated with higher cancer incidence and mortality within countries such as China and India [62]. Additionally, a strong link between selenium deficiency and susceptibility to a variety of viral infections all over the world has been shown. Many researchers have looked at the significance of various types of selenium compounds in preventing enveloped RNA virus infectivity.

https://pubmed.ncbi.nlm.nih.gov/36379313/
Selenium and breast cancer - An update of clinical and epidemiological data 2022
Clinical and epidemiological studies summarized here clearly demonstrate that Se status correlates with breast cancer survival. As a result, one way to curb breast cancer mortality would be via Se supplementation, especially in patients with severely deplete Se status.

https://pubmed.ncbi.nlm.nih.gov/24114479/
Selenium and cancer: a story that should not be forgotten-insights from genomics. 2014
Although epidemiological studies suggest that low Se intake is associated with increased risk of various cancers, the results of supplementation trials have been confusing. These conflicting results may be due to different baseline Se status and/or genetic factors. In addition, mechanistic links between Se intake, selenoproteins and carcinogenesis are not clear. In this article, we discuss the functional significance of single-nucleotide polymorphisms (SNP) in selenoprotein genes and the evidence as to whether or not they influence risk of colorectal, prostate, lung or breast cancers. Both in vitro and in vivo studies have shown that a small number of SNPs in genes encoding glutathione peroxidases 1 and 4, selenoprotein P, selenoprotein S and 15-kDa selenoprotein have functional consequences. Data from case-control studies suggest that a variant at codon 198 in glutathione peroxidase 1 influences the effect of Se status on prostate cancer and risk, and it has also been associated with breast cancer and lung cancer risk, whereas variants in glutathione peroxidase 4, selenoprotein P and selenoprotein S may influence the risk of colorectal cancer. In addition, the results of gene microarray (transcriptomic) studies have identified novel selenoprotein biomarkers of Se status and novel downstream Se-targeted pathways. The work highlights the need to take baseline Se status and genetic factors into account in the design of future intervention trials.

https://pubmed.ncbi.nlm.nih.gov/22294765/
The influence of selenium and selenoprotein gene variants on colorectal cancer risk. 2012
Low intake of the micronutrient selenium (Se) has been implicated as a risk factor in CRC, and in this article we describe the biochemical functions of selenium in selenoproteins, review the evidence for an association of selenium status with CRC and adenoma risk and describe the genetic epidemiological data on selenoprotein genes and CRC risk.

https://pubmed.ncbi.nlm.nih.gov/31027226/
Association of Selenoprotein and Selenium Pathway Genotypes with Risk of Colorectal Cancer and Interaction with Selenium Status. 2019
Selenoprotein genetic variations and suboptimal selenium (Se) levels may contribute to the risk of colorectal cancer (CRC) development. We examined the association between CRC risk and genotype for single nucleotide polymorphisms (SNPs) in selenoprotein and Se metabolic pathway genes.

This study suggests that SNPs in the Se pathway alone or in combination with suboptimal Se status may contribute to CRC development.

https://pubmed.ncbi.nlm.nih.gov/37923090/
Prediagnostic selenium status, selenoprotein gene variants and association with breast cancer risk in a European cohort study. 2023
Selenium (Se) may help prevent breast cancer (BC) development. Owing to limited observational evidence, we investigated whether prediagnostic Se status and/or variants in the selenoprotein genes are associated with BC risk in a large European cohort.
Higher Se status does not appear to be associated with BC risk, although activity of the selenoenzyme GPX3 may be inversely associated with premenopausal BC risk, and SNPs in the Se pathway alone or in combination with suboptimal Se status may influence BC risk.

https://pubmed.ncbi.nlm.nih.gov/30469315/
Expression of Selenoprotein Genes and Association with Selenium Status in Colorectal Adenoma and Colorectal Cancer. 2018
Dietary selenium (Se) intake is essential for synthesizing selenoproteins that are important in countering oxidative and inflammatory processes linked to colorectal carcinogenesis. However, there is limited knowledge on the selenoprotein expression in colorectal adenoma (CRA) and colorectal cancer (CRC) patients, or the interaction with Se status levels. We studied the expression of seventeen Se pathway genes (including fifteen of the twenty-five human selenoproteins) in RNA extracted from disease-normal colorectal tissue pairs, in the discovery phase of sixty-two CRA/CRC patients from Ireland and a validation cohort of a hundred and five CRC patients from the Czech Republic.
Altered selenoprotein expression may serve as a marker of functional Se status and colorectal adenoma to cancer progression.

https://pubmed.ncbi.nlm.nih.gov/38504430/
Serum Selenium Concentration as a Potential Diagnostic Marker for Early-Stage Colorectal Cancer: A Comparative Study. 2024
Selenium deficiency is an established risk factor for colorectal cancer. The aim of the present study was to determine selenium levels in blood samples obtained from colorectal cancer patients compared with the levels of this element in the blood of patients who had undergone hernia repair and cholecystectomy.
CONCLUSIONS This study supports findings from previous studies that low serum selenium levels are associated with colorectal cancer and that selenium deficiency may be a risk factor for colorectal cancer.

https://pubmed.ncbi.nlm.nih.gov/36176217/
Selenium dietary intake and survival among CRC patients. 2023
Despite advances in prevention and treatment, colorectal cancer remains the second most common cause of cancer death. To date, little is known about the role of prediagnostic selenium intake in colorectal cancer survival. Objective: The purpose of the study was to verify whether selenium intake in habitual diet before diagnosis is associated with survival in colorectal cancer patients.
Results: After standardization for several potential confounders (including key determinants, such as radical surgery, chemotherapy, tumor stage, and dietary factors), a decrease in the risk of death from colorectal cancer was observed in the group with higher dietary selenium intake (≥48.8 µg/day, group mean: 63.9 µg/day) compared to the group with lower dietary selenium intake (<48.8 µg/day, mean: 38.5 µg/day) (HR=0.73; 95% CI: 0.54-0.98) (the median was used for categorization). Conclusion: Our study suggests selenium as an additional dietary factor which may be associated with survival among colorectal cancer patients referred to surgery. Due to the observational nature of the study, the results should be taken with caution. These preliminary findings, however, provide the basis for well-structured clinical trials.

https://pubmed.ncbi.nlm.nih.gov/35287753/
Calcium intake may explain the reduction of colorectal cancer odds by dietary selenium - a case-control study in Poland. 2022
Results: After the adjustment for several covariates dietary selenium was associated with the decrease of colorectal cancer odds by 8% (OR = 0.92, 95%CI: 0.84-0.99 for every 10µg Se/day increase). In individuals with lower (< 1000 mg/day) calcium content the odds of colorectal cancer was decreased by 13%(for every 10µg Se/day) and by 44% and 66% depending on the categories of selenium intake (60 to < 80 µg/day and ≥ 80 µg/day, respectively). The effect of dietary selenium was modified by dietary calcium (p for interaction < .005).
Conclusions: The study has shown a beneficial effect of dietary selenium for colorectal cancer and a modification effect of dietary calcium in a population characterized by lower levels of selenium intake. The results provide the basis for well-planned controlled trials to confirm the findings.

https://pubmed.ncbi.nlm.nih.gov/32777945/
Association between Dietary Zinc and Selenium Intake, Oxidative Stress-Related Gene Polymorphism, and Colorectal Cancer Risk in Chinese Population - A Case-Control Study 2021
Zinc and selenium may protect against colorectal cancer (CRC) progression through their anti-oxidative effects. This study examined the independent and combined effect of dietary zinc and selenium intake, and polymorphisms of the oxidative stress-related genes (superoxide dismutase 1, superoxide dismutase 2, glutathione peroxidase, and catalase) on CRC risk in a Chinese case-control study.
Intake of selenium was found to be inversely associated with CRC risk, while zinc was not associated with CRC risk. The ORs (95% CI) for the highest vs. the lowest quartile were 0.42 (95% CI 0.28, 0.64, Ptrend < 0.001) for selenium and 0.96 (95% CI 0.63, 1.47, Ptrend = 0.505) for zinc. Combined effect was observed between zinc and SOD1 rs4998557 on CRC risk (Pinteraction < 0.05).

https://pubmed.ncbi.nlm.nih.gov/28191611/
Vegetarianism and colorectal cancer risk in a low-selenium environment: effect modification by selenium status? A possible factor contributing to the null results in British vegetarians. 2017
Conclusions: Available data on Se intake and status in British vegetarians, as well as the relationship between their secular changes in the UK and changes in CRC risk in this dietary group, are compatible with the hypothesis that low Se status may contribute to the largely null results of studies of CRC risk in vegetarians in the UK.

https://pubmed.ncbi.nlm.nih.gov/36358931/
Metabolism of Selenium, Selenocysteine, and Selenoproteins in Ferroptosis in Solid Tumor Cancers 2022
In this review, we discuss both the evidence and the gaps in knowledge on how cancer cells from solid tumors use Se, Sec, selenoproteins, and the Se-related machinery to promote their survival particularly via resistance to ferroptosis.

https://pubmed.ncbi.nlm.nih.gov/36839209/
An Assessment of Serum Selenium Concentration in Women with Ovarian Cancer 2023
Available studies on the effect of serum selenium levels on the risk of malignancies show some conflicting results. In this study, we investigated the correlation

between serum selenium levels and ovarian cancer occurrence.
Conclusion: The studied patients with ovarian cancer are characterized by statistically significant lower serum selenium levels than patients from the control group. Among the study group, a decrease in selenium concentration was observed with an increase in the FIGO stage. The determination of the role of selenium as a prophylactic factor in ovarian cancer requires further prospective studies.

https://pubmed.ncbi.nlm.nih.gov/28202637/
Supplemental Selenium May Decrease Ovarian Cancer Risk in African-American Women. 2017
activity.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.Conclusions: These findings provide the first insights, to our knowledge, into the potential association between antioxidants and ovarian cancer in African-American women, indicating potential inverse associations with supplemental selenium.

https://pubmed.ncbi.nlm.nih.gov/35267933/
An Assessment of Serum Selenium Concentration in Women with Endometrial Cancer. 2022
Background: Numerous studies have shown a relationship between low serum selenium levels and an increased risk of developing cancer.
Results: The mean concentration of selenium was lower in patients with endometrial cancer than in healthy controls (60.63 μg/L (0.77 μmol/L) vs. 78.74 μg/L (0.99 μmol/L), respectively). When compared in quartiles, a significant association of lower selenium concentration with the incidence of endometrial cancer was recorded.
Conclusion: A strong correlation between the level of selenium in the blood serum and the risk of endometrial cancer indicates that patients with low levels should be a candidate group requiring appropriate preventive examinations. Further research on a larger group of patients is required.

https://pubmed.ncbi.nlm.nih.gov/7707436/
Prospective study of toenail selenium levels and cancer among women. 1995
Background: Inverse associations between selenium status and cancer risk have been observed in animal studies, ecologic studies, and some case-control and prospective studies. Whereas results of some prospective studies have suggested an overall inverse relationship between selenium levels and cancer, other prospective studies have failed to confirm this finding. Prospective data on women are particularly limited because fewer women than men have been studied prospectively.
Conclusions: Toenail selenium levels were not inversely associated with cancer risk in this study.

https://pubmed.ncbi.nlm.nih.gov/34440195/
Serum Selenium Level and 10-Year Survival after Melanoma. 2021
In conclusion, a low serum selenium level was associated with an increased mortality rate in the 10 years following melanoma diagnosis. Future studies in other geographic regions with low soil selenium levels should be conducted to confirm our findings.

https://pubmed.ncbi.nlm.nih.gov/37765058/
Selenium in Prostate Cancer: Prevention, Progression, and Treatment. 2023
Selenium, a trace mineral with various biological functions, has become a focal point in prostate cancer research. This review aims to present a comprehensive overview of selenium's involvement in prostate cancer, covering its impact on prevention, development, treatment, and underlying mechanisms. Observational studies have revealed a link between selenium levels and selenoproteins with prostate cancer progression. However, randomized controlled studies have shown that selenium supplementation does not prevent prostate cancer (HR: 0.95; 95% CI 0.80-1.13). This discrepancy might be attributed to selenoprotein single nucleotide polymorphisms. In the context of combinatorial therapy, selenium has demonstrated promising synergistic potential in the treatment of prostate cancer. Emerging evidence highlights the significant role of selenium and selenoproteins in prostate cancer, encompassing AR signaling, antioxidative properties, cell death, cell cycle regulation, angiogenesis, epigenetic regulation, immunoregulation, epithelial-mesenchymal transformation, and redox signal. In conclusion, selenium's diverse properties make it a promising trace mineral in prostate cancer prevention, development, and treatment and as a platform for exploring novel agents.

https://pubmed.ncbi.nlm.nih.gov/39064692/
A Diet Lacking Selenium, but Not Zinc, Copper or Manganese, Induces Anticancer Activity in Mice with Metastatic Cancers. 2024
A significant improvement in mice survival was observed when the normal diet was replaced with the selenium-free diet. Diets lacking zinc, copper, or manganese showed no significant impact on mice survival. All diets were very well tolerated. The anticancer efficacy of a diet lacking selenium was confirmed in mice with metastatic colon cancer and in mice with metastatic triple-negative breast cancer. These results suggest that diets lacking selenium hold potential for the treatment of metastatic cancers.