Lack of Association between Common Polymorphisms in Selenoprotein P Gene and Susceptibility to Colorectal Cancer, Breast Cancer, and Prostate Cancer: A Meta-Analysis

Hanjiang Xu,1,2,3 Fan Mo,1,2,3 Jun Zhou,1,2,3 Zongyao Hao,1,2,3 Xianguo Chen,1,2,3 and Chaozhao Liang1,2,3
1Department of Urology, The First Affiliated Hospital of Anhui Medical University, Hefei 230000, China
2Institute of Urology, Anhui Medical University, Hefei 230000, China
3Anhui Province Key Laboratory of Genitourinary Diseases, Anhui Medical University, Hefei 230000, China

Correspondence should be addressed to Xianguo Chen; cxg7866186@126.com and Chaozhao Liang; liang_chaozhao@163.com

Received 12 May 2021; Revised 30 August 2021; Accepted 7 September 2021; Published 27 September 2021

Background and Objective. Selenoprotein P (SEPP1) is the major selenoprotein in plasma. Previous studies have demonstrated that SEPP1 expression was reduced in human prostate and colon tumors. Nowadays, studies concerning SEPP1 gene polymorphisms and cancer susceptibility have been extensively investigated, whereas results from these studies remain debatable rather than conclusive. Thus, we performed the present meta-analysis to comprehensively assess the association between two common polymorphisms (rs3877899 and rs7579) in SEPP1 and susceptibility to colorectal, breast, and prostate cancer.

Method. We searched the PubMed, Embase, Google Scholar, and Wanfang (China) databases (up to December 1, 2020) to identify all eligible publications. The pooled odds ratio (OR) correspondence with 95% confidence interval (CI) was calculated to evaluate the associations.

Results. Finally, nine eligible studies with 7,157 cases and 6,440 controls and five studies with 2,278 cases and 2,821 controls were enrolled in rs3877899 and rs7579 polymorphisms, individually. However, a null significant association was detected between the two polymorphisms in SEPP1 and susceptibility to colorectal, breast, and prostate cancer in all comparison models. Subsequently, subgroup analysis based on tumor type, no significant association was identified for prostate, breast, and colorectal cancer. In addition, when the stratification analyses were conducted by the source of control, HWE status, and ethnicity, yet no significant association was found.

Conclusions. The current meta-analysis shows that SEPP1 rs3877899 and rs7579 polymorphisms may not be associated with susceptibility to colon cancer, breast cancer, and prostate cancer, and further well-designed studies with a larger sample size are warranted to validate our findings.

1. Introduction

There has been a progressive increase in the global incidence of malignancies, causing a serious threat to human health, presently, among the main causes of death [1]. Increasing evidence suggests that cancers are multifactorial diseases, which derive from complex coactions between genetic and environmental factors [2].

Oxidative stress, which causes mitochondrial damage and DNA breakage by reactive oxygen species (ROS), is closely related to tumor progression [3, 4]. ROS, like hydrogen peroxide (H2O2), can cause DNA damage due to the continuous production of various cellular metabolic processes in the body, which may lead to malignant transformation of cells [5]. Selenoprotein P (SEPP1) is the dominant selenoprotein in plasma as two isoforms (~50 kDa and ~60 kDa) and is believed to have two main functions: providing tissues with selenium for tissues and exerting antioxidant defense capabilities [6]. The insufficiency of SEPP1 may participate in the occurrence and progression of cancer. Earlier studies have testified high expression of SEPP1 in colonic mucosa and relatively lower expression of SEPP1 in human colon tumors. Moreover, SEPP1 affects colitis-induced tumorigenesis through regulating stemness and...
oxidative damage also has been confirmed in the study [7]. In Calvo et al.’s research, they advanced pointed that the SEPP1 was reduced in prostate cancer (PCa) [8]. Gonzalez-Moreno et al.’s study has shown that knockdown of SEPP1 expression in prostate epithelial neoplasia lesion cell lines and invasive tumors significantly increased ROS and cell growth inhibition after exposure to H₂O₂ [9].

Nowadays, more and more studies have demonstrated that several polymorphisms of the selenoprotein P gene (SEPP1) were associated with susceptibility of tumors, including breast cancer (BC) [10], colorectal cancer (CRC) [11], and PCa [12]. However, results from these studies remain inconclusive. In order to yield a more accurate and robust estimation, we conducted this meta-analysis trying to comprehensively analyze the connection between two common polymorphisms (rs3877899 and rs7579) in SEPP1 and cancer susceptibility.

2. Materials and Methods

2.1. Search Strategy. We conducted this meta-analysis on the basis of the PRISMA meta-analysis guidelines [13]. A comprehensively retrieve of the literature concerning relationships between the SEPP1 polymorphisms and cancer susceptibility was performed on PubMed, Embase, and Google Scholar databases (up to December 1, 2020) by using the following searching terms: "SEPP1 OR Selenoprotein P" AND "polymorphism OR variation OR SNP OR genotype OR allele OR mutation" AND "cancer OR malignancy OR tumor OR neoplasm OR carcinoma". We also conducted manual searches on the references of these selected original studies to identify other eligible studies.

2.2. Inclusion and Exclusion Criteria. Included literature should be in line with the following criteria: (1) studies that evaluated the relationship between SEPP1 polymorphisms (rs3877899 and rs7579) and cancer susceptibility; (2) sufficient genotype data from the text or the supporting information; (3) case-control studies. Moreover, these studies should also be excluded when they were as follows: (1) insufficient data; (2) not a case-control study, such as Comments, Case Reports, and Reviews; (3) the total scores of Newcastle-Ottawa Scale (NOS) is less than 5 (The quality of the enrolled studies was assessed by NOS (Newcastle-Ottawa Scale), which is presented in Table 1). In addition, the specific scoring rules of NOS are listed in Table S1.

2.3. Data Extraction. Two reviewers (Hanjiang Xu and Fan Mo) have devoted themselves to the data extraction process referring to the predetermined criteria. All the discrepancies were settled through discussion till all consensus was settled. Furthermore, the following details should also be extracted: name of the first author, publication year, source of controls, ethnicity of a case-control study, genotype frequencies of cases and controls, and so on.

2.4. Statistical Analysis. We calculated the odds ratio (OR) with 95% CI confidence interval (CI) to appraise the intensity of relationships between SEPP1 polymorphisms (rs3877899 and rs7579) and cancer susceptibility in the following genetic models: allele contrast (A vs. G), recessive (AA vs. AG+GG), dominant (AA+AG vs. GG), heterozygous (AG vs. GG), and homozygous (AA vs. GG) models (G: wild allele; A: variant allele). We assessed the statistical heterogeneity hypothesis through I² statistics to quantify the inconsistency, which represents the proportion of variability between studies that potentially arose from heterogeneity instead of contingency. I² values greater than 50% are considered to have significant heterogeneity [14], indicating the random-effects model would be selected to calculate the pooled OR estimated value of individual study; if not, the fixed-effects model was obtained. Our current study also assessed sensitivity analysis as well as publication bias [15]. We use Stata software for all statistical analysis (version 12.0; STATA Corp, College Station, TX). P ≤ 0.05 was considered statistically significant.

3. Results

3.1. Characteristics of Studies. Overall, 10 publications with 14 independent studies on SEPP1 polymorphisms (rs3877899 and rs7579) and cancer susceptibility were available for our meta-analysis [10, 11, 16–23], and the publication selection process is displayed in Figure 1. For rs3877899 polymorphism, nine case-control studies with 7,157 cases and 6,440 controls met the inclusion criteria, including three BC, two CRC, and four PCa studies. For rs7579 polymorphism, there were five studies (one BC study, one PCa study, and three CRC studies) with 2,278 cases and 2,821 controls that met the eligibility criteria. Cancers were confirmed pathologically or histologically in most studies. The authors of included studies used a variety of genotyping methods, including PCR-RFLP and TaqMan. We think the earlier sentence was correct regarding the genotyping methods used in the included studies. Except for these studies [10, 11, 20, 23], the genotype distribution in control groups of the enrolled studies was in line with HWE. The selected study characteristics are enumerated in Table 2.

3.2. Pooled Analysis. A result of the detailed associations of SEPP1 polymorphisms with cancer susceptibility in all of the genetic models is presented in Table 3. And the results demonstrated that no evidence of the relevance between the two polymorphisms (rs3877899 and rs7579) and susceptibility to CRC, BC, and PCa was found in each genetic model (Table 3).

For rs3877899 polymorphism, no significant association was found when pooling all the eligible studies (A vs. G: OR = 1.099, 95% CI: 0.938-1.287, P = 0.243; AA vs. GG: OR = 1.129, 95% CI: 0.794-1.605, P = 0.498; AG vs. GG: OR = 1.035, 95% CI: 0.909-1.179, P = 0.603; AA+AG vs. GG: OR = 1.079, 95% CI: 0.919-1.267, P = 0.356; AA vs. AG+GG: OR = 1.017, 95% CI: 0.871-1.189, P = 0.555, Table 3). In addition, there was also no significant relationship between rs7579 polymorphism and cancer risk in each genetic models (A vs. G: OR = 1.090, 95% CI: 0.923-1.286, P = 0.309; AA vs. GG: OR = 1.267, 95% CI: 0.861-1.866, P = 0.230; AG vs. GG: OR = 1.022, 95% CI: 0.908-1.151, P = 0.715; AA+AG vs. GG: OR = 1.075, 95% CI: 0.897-1.287, P = 0.434; AA vs. AG+GG: OR = 1.209, 95% CI: 0.878-1.666, P = 0.245, Table 3).
3.3. **Subgroup Analysis.** As to a stratification analysis conducted by cancer type, no association was identified for PCa, BC, and CRC of rs3877899 polymorphism in all five genetic models (Table 3). In addition, we also conducted stratification analyses by the source of control, ethnicity, and HWE status for both two polymorphisms; the null association was detected (Table 3). In all subgroups, the number of included studies is not less than 3 \((n \geq 3)\).

**Table 1: Methodological quality of the included studies according to the Newcastle-Ottawa Scale.**

| Variants | Author          | Representativeness of cases | Source of controls | HWE in controls | Genotyping examination | Association assessment | Total scores |
|----------|-----------------|-----------------------------|--------------------|-----------------|------------------------|------------------------|-------------|
| rs7579   | Meplan et al.   | **                          | **                 | **              | 0                      | **                     | 8           |
|          | Steinbrecher et al. | **                          | **                 | **              | 0                      | **                     | 8           |
| rs3877899 | Meplan et al.  | **                          |                    | **              | 0                      | **                     | 8           |
|          | Steinbrecher et al. | **                          | **                 | **              | 0                      | **                     | 8           |
|          | Cooper et al.   | **                          | **                 | **              | 0                      | **                     | 8           |
|          | Geybels et al.  | **                          | **                 | **              | 0                      | **                     | 8           |
|          | Karunasinghe et al. | **                          | **                 | **              | 0                      | **                     | 8           |
|          | Meplan et al.   | **                          |                    | **              | 0                      | **                     | 5           |
|          | Sutherland et al. | **                          |                    | **              | 0                      | **                     | 7           |
|          | Meplan et al.   | **                          |                    | **              | 0                      | **                     | 5           |
|          | Amini et al.    | **                          |                    | **              | 0                      | **                     | 7           |
|          | Sutherland et al. | **                          |                    | **              | 0                      | **                     | 7           |
|          | Meplan et al.   | **                          |                    | **              | 0                      | **                     | 5           |
|          | Karunasinghe et al. | **                          |                    | **              | 0                      | **                     | 8           |
|          | Mohammaddoust et al. | **                          |                    | **              | 0                      | **                     | 7           |

This table identifies "high" quality choices with a "star." A study can be awarded a maximum of one star for each numbered item within the selection and exposure categories. A maximum of 2 stars can be given for comparability.

**Figure 1: The eligible study selection process.**
The human SEPP gene (SEPP1) contains two functional polymorphisms, rs3877899 (Ala234Thr) and rs7579 (Gram A base mutation in SEPP1 mRNA 3’ UTR), which affect the selenoprotein activity of plasma and lymphocytes and the relative proportion of plasma SEPP isotypes in vivo experiments [26, 27]. Therefore, the mutation of SEPP1 will produce some nonfunctional or low-functional protein subtypes, reducing the antioxidant activity of SEPP1. At the same time, the accumulation of peroxide is conducive to the production and development of cancer. Therefore, mutations in SEPP1 theoretically increase the susceptibility of tumors.

Both polymorphisms of SEPP1 have been reported to be related to the risk of PCa [19] and CRC [20]. Furthermore, in the study conducted by Meplan et al. [18], a connection between the SEPP1 rs3877899 mutation and the risk of BC was also found. However, in a study by Jablonska et al. [22] in Polish women, there was no evidence of a relation between BC risk and the rs3877899 polymorphism. In fact, many related epidemiological studies have been carried out so far, but no definite conclusions have been obtained, and some results are even controversial. Therefore, in order to clarify the relationship between cancer risk and the SEPP1 polymorphism, we conducted this meta-analysis. After pooling all data from 7,157 cases and 6,440 controls for the rs3877899 polymorphism and 2,278 cases and 2,821 controls for the rs7579 polymorphism, a null significant association was identified between SEPP1 polymorphism and cancers (prostate, breast, and colorectal cancer) in all comparative models. We subsequently did subgroup analyses based on cancer type control source HWE status and race for both polymorphisms and found no significant association.

### 3.4. Heterogeneity Evaluation

Table 3 shows that the statistical heterogeneity within studies was evaluated by a chi-squared-based Q-statistic test. When \( P > 0.10 \), the fixed-effects model (the Mantel-Haenszel model) was used; else, the random-effects model (the DerSimonian-Laird model) was adopted.

### 3.5. Sensitivity Analysis and Publication Bias

We explored the impact of each study on the pooled OR by excluding one study from the pooled analysis, thereby performing a sensitivity analysis. It turns out there is no material influence on the stability of the results. So as to assess the publication bias of the existing literature, we performed Begg’s funnel plot as well as Egger’s test. In all comparison models, the pattern of the funnel chart was roughly symmetrical (Figures 2(a) and 2(b)). In addition, we also used the Egger test, and these results indicated no publication bias (Table 3).

### 4. Discussion

SEPP1 plays an important role in both supplying selenium to tissues and exerting antioxidant defenses. The delivery of selenium is accomplished by the C-terminal domain of SEPP1, which includes nine selenocysteine residues, while antioxidation is accomplished by selenocysteine that has been shown to have peroxidase activity [24]. The antioxidant function of SEPP1 suggests that it has the effect of preventing cancer, especially in inflammatory cancer characterized by increased oxidative stress [25]. Dysfunction of SEPP1 may contribute to the occurrence and progression of cancer.
Table 3: Subgroup analyses of the SEPP1 polymorphisms and cancer risk.

| Variants | Comparison | Subgroup | N | \(P_H\) | \(P_L\) | \(P_E\) | Regression model |
|----------|------------|----------|---|-------|-------|-------|-----------------|
|          |            |          |   | \(P_{\text{value}}\) |       |       | Random | Fixed |
| **rs3877899** |            |          |   |       |       |       |       |       |
| A vs. G  | Overall    | 9        | ≤0.001 | 0.243 | 0.104 | 1.099 | (0.938-1.287) | 1.008 | (0.948-1.071) |
| A vs. G  | PCa        | 4        | 0.514  | 0.206 |       | 0.954 | (0.885-1.027) | 0.953 | (0.885-1.027) |
| A vs. G  | BC         | 3        | ≤0.001 | 0.240 |       | 1.480 | (0.770-2.844) | 1.134 | (0.992-1.295) |
| A vs. G  | PB         | 7        | ≤0.001 | 0.335 |       | 1.093 | (0.912-1.310) | 0.993 | (0.931-1.059) |
| A vs. G  | Y          | 7        | 0.293  | 0.231 |       | 0.962 | (0.888-1.042) | 0.961 | (0.899-1.026) |
| A vs. G  | European   | 7        | 0.269  | 0.434 |       | 0.979 | (0.910-1.055) | 0.976 | (0.917-1.038) |
| AA vs. GG| Overall    | 8        | ≤0.001 | 0.498 | 0.337 | 1.129 | (0.794-1.605) | 1.021 | (0.871-1.196) |
| AA vs. GG| PCa        | 4        | 0.206  | 0.604 |       | 0.946 | (0.718-1.246) | 0.949 | (0.780-1.155) |
| AA vs. GG| BC         | 3        | ≤0.001 | 0.405 |       | 1.726 | (0.478-6.237) | 1.269 | (0.902-1.784) |
| AA vs. GG| PB         | 7        | ≤0.001 | 0.483 |       | 1.162 | (0.765-1.765) | 1.020 | (0.861-1.210) |
| AA vs. GG| Y          | 6        | 0.081  | 0.599 |       | 0.925 | (0.693-1.236) | 0.917 | (0.767-1.095) |
| AA vs. GG| European   | 7        | 0.124  | 0.397 |       | 0.936 | (0.738-1.187) | 0.931 | (0.790-1.098) |
| AG vs. GG| Overall    | 9        | 0.036  | 0.603 | 0.109 | 1.035 | (0.909-1.179) | 1.003 | (0.928-1.084) |
| AG vs. GG| PCa        | 4        | 0.585  | 0.156 |       | 0.934 | (0.850-1.027) | 0.934 | (0.850-1.026) |
| AG vs. GG| BC         | 3        | 0.046  | 0.203 |       | 1.300 | (0.868-1.947) | 1.123 | (0.948-1.331) |
| AG vs. GG| PB         | 7        | 0.072  | 0.975 |       | 0.998 | (0.875-1.138) | 0.976 | (0.898-1.060) |
| AG vs. GG| Y          | 7        | 0.478  | 0.351 |       | 0.960 | (0.883-1.044) | 0.961 | (0.884-1.045) |
| AG vs. GG| European   | 7        | 0.308  | 0.703 |       | 0.989 | (0.904-1.082) | 0.985 | (0.911-1.065) |
| AG+AA vs. GG| Overall  | 9        | 0.001  | 0.356 | 0.098 | 1.079 | (0.919-1.267) | 1.008 | (0.936-1.085) |
| AG+AA vs. GG| PCa    | 4        | 0.623  | 0.152 |       | 0.936 | (0.855-1.025) | 0.936 | (0.855-1.025) |
| AG+AA vs. GG| BC     | 3        | ≤0.001 | 0.210 |       | 1.474 | (0.804-2.704) | 1.150 | (0.980-1.350) |
| AG+AA vs. GG| PB     | 7        | 0.001  | 0.551 |       | 1.056 | (0.884-1.261) | 0.984 | (0.909-1.064) |
| AG+AA vs. GG| Y      | 7        | 0.452  | 0.266 |       | 0.955 | (0.881-1.034) | 0.956 | (0.882-1.035) |
| AG+AA vs. GG| European| 7        | 0.317  | 0.553 |       | 0.981 | (0.901-1.068) | 0.978 | (0.907-1.054) |
| AA vs. AG+GG| Overall| 8        | 0.001  | 0.555 | 0.371 | 1.103 | (0.797-1.526) | 1.017 | (0.871-1.189) |
| AA vs. AG+GG| PCa    | 4        | 0.176  | 0.811 |       | 0.974 | (0.733-1.295) | 0.977 | (0.806-1.184) |
| AA vs. AG+GG| BC     | 3        | ≤0.001 | 0.445 |       | 1.580 | (0.489-5.108) | 1.199 | (0.856-1.681) |
| AA vs. AG+GG| PB     | 7        | 0.001  | 0.497 |       | 1.143 | (0.777-1.681) | 1.027 | (0.869-1.215) |
| AA vs. AG+GG| Y      | 6        | 0.067  | 0.699 |       | 0.944 | (0.704-1.265) | 0.936 | (0.786-1.115) |
| AA vs. AG+GG| European| 7        | 0.113  | 0.444 |       | 0.940 | (0.741-1.192) | 0.939 | (0.799-1.103) |
| **rs7579** |            |          |   |       |       |       |       |       |
This result contradicts our previous theoretical speculation. In fact, SEPP1 polymorphism affects tumor susceptibility through the antioxidant activity of SEPP1 protein. However, there may be more than one factor that can change the antioxidant activity of SEPP1 protein. The study by Sutherland et al. [23] showed that the two polymorphisms of SEPP1 (rs3877899 and rs7579) are not associated with the risk of CRC, which may be due to the inconsistent
dietary selenium intake of the subjects. It is possible that when the plasma selenium level is low, the difference in the plasma level of SEPP1 caused by genetic polymorphism can be reflected, and this difference will disappear after selenium supplementation [26]. Furthermore, our results can be analyzed more accurately by age, cancer grade, and environmental factors (such as selenium status related to SEPP1 expression). For example, in the study of Cooper et al. [21], cancer was divided into two groups of nonprogressive and progressive, and even the factor of smoking was included. Therefore, to explore the impact of genotype on cancer susceptibility, environmental and nutritional factors should be strictly controlled; otherwise, the results may be biased.

In conclusion, despite providing a sufficient statistical sample size to enhance the reliability of our findings, there are some shortcomings of the study. Firstly, the relatively small number of included studies would be a limitation and may constrain our conclusions. Secondly, we only searched papers published in a limited number of databases and some studies may have been overlooked. Finally, the results may be false negative, because some included studies show a significant relation between SEPP1 polymorphism and cancer susceptibility.

5. Conclusions

In this meta-analysis, our results find no association between SEPP1 rs3877899 and rs7579 polymorphisms and susceptibility to CRC, BC, and PCA. Taking into account the complex interactions between genes and the environment, it is necessary to conduct unbiased studies with more sample sizes and more cancer types in different ethnic groups.

Data Availability

The dataset can be accessed from the corresponding author upon reasonable request.

Disclosure

The funders had no roles in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Conflicts of Interest

All authors declared that there is no competing interest.

Authors’ Contributions

H.X. and F.M. accessed information from the literature for this article. J.Z., Z.H., X.C., and C.L. contributed towards writing, discussing, and editing the manuscript. Hanjiang Xu and Fan Mo contributed equally to the work.

Acknowledgments

This work was supported by the Clinical Key Subjects Program of the Ministry of Public Health (Urology), the National Natural Science Foundation of China (81170698, 81370856, and 81401518), the Key Science and Technology Program of Anhui Province (12010402128), the Anhui Provincial Natural Science Foundation (1408085QH180), and the cultivation project for NSFC at Anhui Medical University (2013KJ14).

Supplementary Materials

Table S1: scale for quality assessment. (Supplementary Materials)

References

[1] F. Bray, J. Ferlay, I. Soerjomataram, R. L. Siegel, L. A. Torre, and A. Jemal, “Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries,” CA: a Cancer Journal for Clinicians, vol. 68, no. 6, pp. 394–424, 2018.
[2] M. Carbone, S. T. Arron, B. Beutler et al., “Tumour predisposition and cancer syndromes as models to study gene-environment interactions,” Nature Reviews. Cancer, vol. 20, no. 9, pp. 533–549, 2020.
[3] U. S. Srinivas, B. W. Q. Tan, B. A. Vellayappan, and A. D. Jeyasekharan, “ROS and the DNA damage response in cancer,” Redox Biology, vol. 25, article 101084, 2019.
[4] Y. Yang, S. Karakhanova, W. Hartwig et al., “Mitochondria and mitochondrial ROS in cancer: novel targets for anticancer therapy,” Journal of Cellular Physiology, vol. 231, no. 12, pp. 2570–2581, 2016.
[5] Ö. Canli, A. M. Nicolas, J. Gupta et al., “Myeloid cell-derived reactive oxygen species induce epithelial mutagenesis,” Cancer Cell, vol. 32, no. 6, pp. 869–883.e5, 2017.
[6] Y. Saito, “Selenoprotein P as an \(<\text{in vivo}>\text{redox regulator: disorders related to its deficiency and excess,}\) Journal of Clinical Biochemistry and Nutrition, vol. 66, no. 1, pp. 1–7, 2020.
[7] O. H. al-Taie, N. Uceyler, U. Eubner et al., “Expression profiling and genetic alterations of the selenoproteins GI-GPx and SePP in colorectal carcinogenesis,” Nutrition and Cancer, vol. 48, no. 1, pp. 6–14, 2004.
[8] A. Calvo, N. Xiao, J. Kang et al., “Alterations in gene expression profiles during prostate cancer progression: functional correlations to tumorigenicity and down-regulation of selenoprotein-P in mouse and human tumors,” Cancer Research, vol. 62, no. 18, pp. 5325–5335, 2002.
[9] O. Gonzalez-Moreno, N. Boque, M. Redrado et al., “Selenoprotein-P is down-regulated in prostate cancer, which results in lack of protection against oxidative damage,” The Prostate, vol. 71, no. 8, pp. 824–834, 2011.
[10] S. Mohammaddoust, Z. Salehi, and H. Saedi Saedi, “SEP-P1andSEP15gene polymorphisms and susceptibility to breast cancer,” British Journal of Biomedical Science, vol. 75, no. 1, pp. 36–39, 2018.
[11] G. Amini, R. Salehi, A. Moshtagh, M. Kazemi, M. Behjati, and S. Khosravi, “Evaluation of SEPP1 and selenoprotein S gene polymorphisms (rs 7579 and rs 34713741) in relation to colorectal cancer susceptibility in subset of Iranian population: a case-control study,” Advanced Biomedical Research, vol. 8, no. 1, p. 47, 2019.
12] W. Xie, M. Yang, J. Chan et al., “Association of genetic variations of selenoprotein genes, plasma selenium levels, and prostate cancer aggressiveness at diagnosis,” The Prostate, vol. 76, no. 7, pp. 691–699, 2016.

13] D. Moher, A. Liberati, J. Tetzlaff, D. G. Altman, and PRISMA Group, “Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement,” Journal of Clinical Epidemiology, vol. 62, no. 10, pp. 1006–1012, 2009.

14] J. P. T. Higgins and S. G. Thompson, “Quantifying heterogeneity in a meta-analysis,” Statistics in Medicine, vol. 21, no. 11, pp. 1539–1558, 2002.

15] M. B. Mathur and T. J. VanderWeele, “Sensitivity analysis for publication bias in meta-analyses,” Journal of the Royal Statistical Society. Series C, Applied Statistics, vol. 69, no. 5, pp. 1091–1119, 2020.

16] N. Karunasinghe, D. Y. Han, M. Goudie et al., “Prostate disease risk factors among a New Zealand cohort,” Journal of Nutrigenetics and Nutrigenomics, vol. 5, no. 6, pp. 339–351, 2012.

17] M. S. Geybels, C. M. Hutter, E. M. Kwon et al., “Variation in selenoenzyme genes and prostate cancer risk and survival,” The Prostate, vol. 73, no. 7, pp. 734–742, 2013.

18] C. Méplan, L. O. Dragsted, G. Ravn-Haren, A. Tjønneland, U. Vogel, and J. Hesketh, et al., “Association between polymorphisms in glutathione peroxidase and selenoprotein P genes, glutathione peroxidase Activity, HRT Use and Breast Cancer Risk,” PloS ONE, vol. 8, no. 9, article e73316, 2013.

19] A. Steinbrecher, C. Méplan, J. Hesketh et al., “Effects of selenium status and polymorphisms in selenoprotein genes on prostate cancer risk in a prospective study of European men,” Cancer Epidemiology and Prevention Biomarkers, vol. 19, no. 11, pp. 2958–2968, 2010.

20] C. Meplan, D. J. Hughes, B. Pardini et al., “Genetic variants in selenoprotein genes increase risk of colorectal cancer,” Carcinogenesis, vol. 31, no. 6, pp. 1074–1079, 2010.

21] M. L. Cooper, H. O. Adami, H. Gronberg, F. Wiklund, F. R. Green, and M. P. Rayman, “Interaction between single nucleotide polymorphisms in selenoprotein P and mitochondrial superoxide dismutase determines prostate cancer risk,” Cancer Research, vol. 68, no. 24, pp. 10171–10177, 2008.

22] E. Jablonska, J. Gromadzinska, B. Peplonska et al., “Lipid peroxidation and glutathione peroxidase activity relationship in breast cancer depends on functional polymorphism of GPX1,” BMC Cancer, vol. 15, no. 1, 2015.

23] A. Sutherland, D. Kim, C. Relton, Y. Ahn, and J. Hesketh, “Polymorphisms in the selenoprotein S and 15-kDa selenoprotein genes are associated with altered susceptibility to colorectal cancer,” Genes & Nutrition, vol. 5, no. 3, pp. 215–223, 2010.

24] R. F. Burk and K. E. Hill, “Selenoprotein P—Expression, functions, and roles in mammals,” Biochimica et Biophysica Acta (BBA) - General Subjects, vol. 1790, no. 11, pp. 1441–1447, 2009.

25] C. W. Barrett, S. P. Short, and C. S. Williams, “Selenoproteins and oxidative stress-induced inflammatory tumorigenesis in the gut,” Cellular and Molecular Life Sciences, vol. 74, no. 4, pp. 607–616, 2017.

26] C. Méplan, L. K. Crosley, F. Nicol et al., “Genetic polymorphisms in the human selenoprotein P gene determine the response of selenoprotein markers to selenium supplementation in a gender-specific manner (the SELGEN study),” The FASEB Journal, vol. 21, no. 12, pp. 3063–3074, 2007.

27] C. Méplan, F. Nicol, B. T. Burtle et al., “Relative abundance of selenoprotein P isoforms in human plasma depends on genotype, se intake, and cancer status,” Antioxid Redox Signal, vol. 11, no. 11, pp. 2631–2640, 2009.