Supplementary Material

# Supplementary Figures and Tables

## Supplementary Figures



**Supplementary Figure 1.** PRISMA flow diagram

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Author/Year | Studydesign | Country | Main Content | Cancertype | Stage | Treatment | Mean age±SD | Sample size | Measurement | Gene type | Outcome(mean±SD/OR/95%CI) | *P* value |
| Aline Hajj 2022(20) | Cross-sectional | the Middle East | The aim of this study was to assess the severity of cancer-related fatigue in a group of breast cancer patients undergoing chemotherapy and explore the association between fatigue scores and sociodemographic, clinical, biological, psychiatric, and genetic factors. | breast cancer | NR | Chemo | 56.22±11.96 | 67 | EORTC QLQ-C30 | COMT rs4680 VVCOMT rs4680 VMCOMT rs4680 MMDRD2 rs6277 CCDRD2 rs6277 CTDRD2 rs6277 TTOPRM1 rs1799971 MOPRM1 rs1799971 AGCLOCK rs1801260 TTCLOCK rs1801260 TCPER2 rs934945 GGPER2 rs934945 GAPER2 rs934945 AACRY2 rs10838524 GGCRY2 rs10838524 AGCRY2 rs10838524 AAABCB1 rs1045642 CCABCB1 rs1045642 CTABCB1 rs1045642 TT | 42.59±35.828.77±28.7747.92±3659.26±31.4342.59±31.0334.52±31.7743.16±31.439.68±36.3642.59±33.243.75±30.2637.78±32.7948.79±30.4755.56±38.4944.44±31.844.09±32.2635.04±34.536.36±26.834.29±34.2938.68±32.67 | *p* =0.814*p*=0.128*p*=0.637*p*=0.933*p*=0.318*p*=0.564*p*=0.572 |
| B. Cameron 2021(21) | Cohort | Australia | Cancer-related fatigue, mood disturbances, pain and cognitive disturbance are common after adjuvant cancer therapy, but vary considerably between individuals despite common disease features and treatment exposures. A genetic basis for this variability was explored in a prospective cohort. | breast cancer | III | Surgery：123Chemo：136RT:146 | 52.8±10.1 | 210 | / | s1800896 IL-10-1082 rs1800795 IL-6 -174 | Dominant model0.29 0.09–0.95Recessive model0.36 0.13–0.980.27 0.10–0.75 | *p* =0.041*p* =0.046*P*=0.012 |
| Xiao 2018(22) | Cross-sectional | America | The aim of this study is to determine the relationship between fatigue and specific gene expression profiles associated with inflammation in human papillomavirus (HPV)-related and -unrelated HNC patients undergoing treatment. | head and neck cancer | ≤IIIIV | RT：3RT＋Surgery：7RT＋Chemo：21RT＋Chemo＋Surgery：13 | 59.05±10.39 | 44 | Multidimensional Fatigue Inventory (MFI) 20-item | NF-kBIRF | 1.45±SE0.45-1.25±0.48 | *p* =0.001*p* =0.010 |
| Xi 2018(23) | Cross-sectional | China | To explore the correlation between the SERT gene promoter single nucleotide polymorphisms (SNPs) rs25531 and rs956304 and the cancer-related fatigue (CRF) of colon and rectal cancer, and also to analyze the correlation of the interaction of genetic and non-genetic factors. | colon and rectal cancer | IIIIIIV | NR | ≤60 304＞60 264 | 568 | Brief Fatigue Inventory (BFI-C) | SNPrs25531AG＋GG | 1.77 1.22–2.59 | *p*＜0.001 |
| T. Kühl 2018(24) | Cohort | Germany | This study aimed to validate previously reported associations using the largest independent breast cancer sample to date and to evaluate further functional cytokine variants in relation to total CRF and all relevant CRF subdomains (physical, cognitive, and affective CRF). | breast cancer | 1234 | Surgery | 63 | 684 | Fatigue Assessment Questionnaire | TNF α rs3093662  | Additive 2.38 1.29–4.39Dominant2.47 1.30–4.70 | *p* =0.01*p* =0.006 |
| TerriS. Armstrong 2018(25) | Cross-sectional | America | The purpose of this study was to explore genetic variants associated with moderate to severe fatigue in patients with glioma. | glioma | IIIIIV | Surgery | None-Mild45±13Moderate-Severe48±13 | 176 | the Functional Assessment of Cancer Therapy-Brain (FACT-BR) | ARNTL2 rs922270CLOCK rs3792603PER1 rs2253820PER2 rs934945 | OR：1.8691.5990.6040.614 | *p* = 0.033*p* = 0 .059*p* = 0 .089*p* < 0.100 |
| Jasmine Eshragh 2017(26) | Cohort | America | In patients with breast cancer, variations in neurotransmitter genes between Lower and Higher Fatigue latent classes and between the Higher and Lower Energy latent classes were evaluated. | breast cancer | 0IIIIII | Surgery | Lower Fatigue57.8±11.9Higher Fatigue53.1±11 | 397 | Lee Fatigue Scale (LFS) | ARDB2rs1042718BDNFrs6265COMTrs9332377CYP3A4rs4646437GCH1rs3783642 | 0.030-0.5820.278-0.8970.256-0.9190.253-0.9140.260-0.859 | *p*=0.008*p*=0.020*p*=0.026*p*=0.025*p*=0.014 |
| Luo 2017(27) | Cross-sectional | China | Analyze the association between susceptibility to chemotherapy-related fatigue in colorectal cancer patients and polymorphisms in the promoter region of the serotonin transporter gene (5-HTTLPR), specifically focusing on the long (LL) and short (SS) variants, as well as the heterozygous (LS) genotype. | colon and rectal cancer | IIIIIIV | Chemo | / | 121 | Brief Fatigue Inventory (BFI-C) | 5-HTTLPR | LS 3.580 0.731-17.541SS 8.255 1.694-39.927 | *p* =0.116*p* =0.009 |
| Xiao 2016(28) | Cohort | America | Patients with head and neck cancer (HNC) receiving intensity-modulated radiation therapy (IMRT) have particularly high rates of fatigue, and pre- and post-radiotherapy fatigue are prognostic factors for pathologic tumor responses and poor survival. | Head and neck cancer | ≤IIIIV | RT：1RT＋Surgery：7RT＋Chemo：34RT＋Chemo＋Surgery：4 | 57.76 ±10.44 | 46 | Multidimensional Fatigue Inventory (MFI) 20-item | IL6sTNFR2CRP | 8.04±8.674.49±2.379.59±15.44 | *p*=0.0013*p*＜0.0001*p*=0.6590 |
| Kord M. Kober 2016(29) | Cohort | America | To identify subgroups (i.e., latent classes) of women with distinct fatigue and energy trajectories; evaluate for differences in phenotypic characteristics between the latent classes for fatigue and energy; and evaluate for associations between polymorphisms in genes for pro- and anti-inflammatory cytokines, their receptors, and their transcriptional regulators and latent class membership. | breast cancer | 0IIIIIIIV | Surgery | Lower Fatigue 57.8Higher Fatigue 53.1 | 516 | Karnofsky Performance Status (KPS) scale | IL1Brs16944IL10rs3024496 | 1.336-6.2260.172-0.682 | *p*=0.08*p*=0.02 |
| Anand Dhruva 2015(30) | Cross-sectional | America | The purpose of this study was to evaluate for differences in variations in pro- and antiinflammatory cytokine genes between participants who were classified as having low and high levels of morning and evening fatigue and to evaluate for differences in phenotypic characteristics between these two groups. | breast, prostate, lung, or brain cancer | NR | RT | 61.5 | 252 | Lee Fatigue Scale (LFS), | TNFArs1800629TNFArs3093662IL4rs2243248TNFArs2229094 | 0.252-0.9101.796-24.1710.120-0.7621.389-10.110 | *p*=0.025*p*=0.004*p*=0.011*p*=0.009 |
| Cielito C. Reyes-Gibby 2013(31) | Cross-sectional | America | We applied novel statistical methods to assess whether variants of 37 inflammation genes may serve as biologic markers of risk for severe pai》 | non-small cell lung cancer | I-IIIAIIIB-IV | NR | 61±12 | 97 | 12-Item Short-Form Health Survey (SF-12) | IL-8-T251 AIL-10 | 2.07 1.16-3.700.49 0.25-0.92 | *p*=0.014*p*=0.028 |
| Fernandez 2012(32) | Cross-sectional | Spain | Our aim was to examine the influence of catechol-O-methyltransferase (COMT) Val158Met genotypes on cancer-related fatigue, postmastectomy pain, and pressure pain hypersensitivity in breast cancer survivors.. | breast cancer | I-IIIA | Surgery | 25-65 | 128 | Piper fatigue scale (PFS) | COMT Val/ValCOMT Val/MetCOMT Met/Met | 4.8±1.7（4.1-5.4）5.9±1.7（5.5-6.4）6.4±1.6（5.8-7.0） | *p*＜0.001 |
| Alicia 2008(33) | Case-control | America | We examined single nucleotide polymorphisms (SNPs) in the promoters of cytokine genes as genetic risk factors for cytokine-related fatigue in 33 fatigued and 14 non-fatigued breast cancer survivors, focusing on promoter sequence polymorphisms in IL1B and IL6 associated with differential expression of proinflammatory cytokines. | breast cancer | 0III | Chemo | Fatigued54.1 ± 8.3Non-fatigued61.1 ± 8.5 | 47 | vitality subscale of the SF-36 | IL 1B −511（C/T）IL 6 −174（G/C） | 0.91-16.6 1.12-17.9  | *p*=0.007*p*=0.027 |

**Supplementary Table 1.**Characteristics of the included studies.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Author/Year | Year | Study design | Mean age | Sample size | JBI quality assessment outcome |
| Aline Haj(20) | 2022 | Cross- sectional | 56.22±11.96 | 67 | High |
| B. Cameron(21) | 2021 | Cohort | 52.8±10.1 | 111 | Low |
| Canhua Xiao(22) | 2018 | Cohort | 59.05±10.39 | 44 | Medium |
| Xi Ouyang(23) | 2018 | Cross- sectional | N/A | 568 | High |
| T. Kühl(24) | 2018 | Cohort | 63 | 684 | High |
| Terri S. Armstrong(25) | 2018 | Cross- sectional | Mild group45±13Severe group48±13 | 176 | Medium |
| Jasmine Eshragh(26) | 2017 | Cohort | Low fatigue57.7±11.9High fatigue53.1±11 | 397 | Medium |
| Luo(27) | 2017 | Cross- sectional | N/A | 121 | High |
| Canhua Xiao(28) | 2016 | Cohort | 57.76 ±10.44 | 46 | High |
| Kord M. Kober(29) | 2016 | Cohort | 57.8/53.1 | 516 | High |
| Anand Dhruva(30) | 2015 | Cross- sectional | 61.5 | 252 | High |
| Cielito C. Reyes-Gibby | 2013 | Cross- sectional | 61±12 | 97 | High |
| Ce´sar(31)Ferna´ndez-de-las-Pen˜as(32)  | 2012 | Cross- sectional | 25-65 | 128 | High |
| Alicia Collado-Hidalgo(33) | 2008 | Cohort | 54.1 ± 8.3 | 47 | High |

**Supplementary Table 2.** Quality Assessment.