ISSN Online: 3007-1941 ISSN Print: 3007-1933 https://msra.online/index.php/Journal/about

Multidisciplinary Surgical Research Annals
https://msra.online/index.php/Journal/about
Volume 3, Issue 2 (2025)

Analysis of Genetic Polymorphism Association of Interleukin-8 (+781 C/T) in Breast Cancer Patients

Muhammad Talha Akhtar[1*], Sumaira Aziz[1], Muhammad Ishfaq[2], Amber Aftab Khan[3], Muhammad Aziz[4], Faiza Zubair[5], Anam Amir[6], Syed Sajid Hussain Shah[7], Syed Sami Ahmad Samar Bukhari[8]

Article Details

Keywords: Molecular basis of breast cancer, IL-8 and SNP, Genetic polymorphism, PCR, Gel Electrophoresis

[1]**Muhammad Talha Akhtar**
Department of Biotechnology, University of Sargodha, Pakistan
[2]**Sumaira Aziz**
Department of Biotechnology, University of Sargodha, Pakistan
[3]**Muhammad Ishfaq**
Department of Medical Laboratory Sciences, The University of Lahore, Pakistan
[4]**Amber Aftab Khan**
Department of Biological Science, Superior University Lahore, Sargodha Campus
[5]**Muhammad Aziz**
Department of Zoology, Islamia College Peshawar, Pakistan
[6]**Faiza Zubair**
Department of Zoology, University of Sargodha, Pakistan
[7]**Anam Amir**
Department of Life Sciences, University of Management and Technology, Lahore
[8]**Syed Sajid Hussain Shah**
Department of Zoology, University of Okara, Pakistan
[9]**Syed Sami Ahmad Samar Bukhari**
Department of Allied Health Sciences, Superior University Lahore, Sargodha Campus

ABSTRACT

Globally, Breast cancer is the major mortality risk among the females. Its complex etiology includes a variety of risk factors, including genetic predisposition. Interleukin-8 (IL-8), a chemoattractant, has received attention for its possible prognostic and histopathological importance in breast cancer. The aim of this research was to look at the relationship between environmental variables, genetic variation (IL-8, +781 C/T) polymorphism, and breast cancer in Pakistan. The study had two goals: first, to examine the impact of environmental variables on breast cancer risk, and second, to investigate the IL-8 (+781 C/T) polymorphism and breast cancer relationship susceptibility. Samples of blood in this study group were taken from 100 breast cancer patients and 50 healthy control females across several institutions using a thorough case-control methodology. Specific primers were used to amplify the SNP through PCR; and agarose gel electrophoresis were used to genotype the IL-8 (+781 C/T) polymorphism. In breast cancer patients, the genotype distribution revealed that 67% had the CT genotype, and 33% had the TT genotype. The T allele was more common in both groups, accounting for 66.5%. The findings revealed a favorable relationship between age and CRP (r = 0.387***) as well as CTC (r = 0.369***). Notably, CRP correlated positively with CTC (r = 0.270***), indicating a reciprocal impact between both variables. According to the findings of this extensive study, the CT genotype was substantially more prevalent in breast cancer patients with the IL-8 +781 C/T polymorphism. Individuals with the TT genotype of IL-8 +781 C/T were shown to be more sensitive to breast cancer.

Introduction

One of typical diseases is the tumor of breast on this planet, with about 2.3 million females identified in the last five years, contributing to 685,000 deaths worldwide by 2020 (Peng, Madduri, Clontz, & Stewart, 2023). Breast carcinoma poses a severe threat to global health since it is often identified condition and considered major cause of mortality risk of cancer in practically all women worldwide. Higher rates of breast cancer are seen in more developed areas, and this breast carcinoma incidence is directly connected with human development. However, because of their larger populations, developed and developing countries see a diagnosis rate of more than 50% of breast cancer cases. Age, reproductive variables, obesity, alcohol consumption, and genetic abnormalities are the major risk key factors for this serious breast carcinoma (Noor et al., 2024).

Breast cancer survival rates differ in accordance with the level of development in the area. High survival rates can be due to early discovery and access to efficient treatments in more industrialized nations. In contrast, diagnosis takes longer in less developed areas. IL-8 is also a commonly studied pro-inflammatory biomarker in breast tumor research. IL-8 levels were measured in three of the five studies that measured, it was discovered that less IL-8 levels are interlinked with greater complete survival (Z. Y. Zhu et al., 2018). Patients with less IL-8 expression in therapy combining the monoclonal antibodies camrelizumab and apatinib (Liu et al., 2021). Furthermore, it was discovered that a minute quantity of IL-8 plasma levels afterward treatment possibly indicates improved overall lengthy survival (Tiainen et al., 2019).

Researchers discovered that it has been seen that IL-8 level rise significantly reduced following therapy, as one of the signs of a less inflammatory state in those with breast cancer, in a study using a conventional three "cooling" herbs of Chinese combination of, San Huang decoction, recognized for successfully alleviating injury-related inflammation and pain (J. Zhu & Paul, 2008). Confirmed the beneficial combination between BMI and IL-8 by two additional studies but failed to explain how this association may influence the course of the disease (Ramirez et al., 2017); another research investigated whether inflammatory variables could have exercise habit impacts on quality of sleep in breast cancer individuals who survive although found no significant influence of levels of IL-8, by resulting that this indication by itself would not enough to as a result in sleep-related results (Rogers et al., 2015). American Cancer Society of Breast Cancer (Giaquinto et al., 2022). Facts & figures ranging from 2017 to 2018 revealed that breast cancer pathophysiology is complex and still insufficiently understood, however, several risk factors are identified.

The most prevalent risk factors are increasing age and feminine gender. Genetic abnormalities are the cause of 10% of Breast cancers, namely BRCA 1 and 2. A past diagnosis of ductal carcinoma in situ, In addition to known risk factors, include a high BMI, first pregnancy after the age of 30 or nulliparity, premature menarche (before the age of 13), relatives of breast or ovarian cancer history, post-menopause, and utilization of postmenopausal hormonal therapy. More thick breasts and women with white colure and ladies with a normal BMI are most in danger amongst hormonal treatment who are postmenopausal users. Females who have had previous breast radiotherapy are likely to a more dangerous (Hou et al., 2013).

According to Studies of Endogenous Hormones and Breast Cancer Collaborative Group (2011), Poor diet is also a main concern for certain type of cancers, like fifty percent leads to breast cancer, similar for cancer of gall bladder and endometrial cancer as well as cancer of pancreases, cancer of colorectal and prostate are 70% and 75% respectively. The four major subtypes of breast cancer have distinct histologists and indications as well as diagnoses. Breast cancer is grouped based on anatomic presence (lobular or ductal), activity of human epidermal growth factor receptor 2 (HER-2) and receptive capability of hormones (Howlader et al., 2014). Progesterone as well as oestrogen receptor expression inside the tumors can be present or absent depending on its hormone responsiveness. In cases of hormone-receptor having active cancer inside the breast, hormone-blocking treatment is believed to be beneficial, particularly when the tumor is not metastatic. HER-2-positive tumors usually respond to HER-2-targeted monoclonal antibodies. The most common expression status in breast cancer is hormonal receptor positive as well as HER-2 negative. Lack of HER-2 expression or hormone responsiveness are two characteristics of triple-negative breast cancer. 12 percent of breast cancer patients in women will have

triple-negative disease, according to a survey. Triple-negative disease is considered highly frequent in different age groups of black women of non-Hispanic black, rather it can be identified at a younger age as compared to other subtypes. Female patients having triple-negative illness have more chances to be diagnosed later in the disease's progression (stage III or IV) (Howlader et al., 2014). A cytokine called interleukin-8 (IL-8) is essential for the emergence and spread of breast cancer.

In the tumor microenvironment, stromal cells and cancer cells both produce IL-8, which is engaged in a number of critical events that increases the growth and metastasis of certain tumor and structure analysis. Understanding the functionality of IL-8 in breast cancer can lead to the discovery of advanced treatment targets and enhance patient prognosis (Y. C. Wang et al., 2022). Immune cells are drawn to the tumor microenvironment by IL-8, which helps to create an inflammatory response (Lin, 2017). IL-8 has also been shown in studies to affect the functionality of immune cells including T cells and natural killer cells, inhibiting the immunity response and increasing tumor growth (X. Wang & Cheng, 2020).

Furthermore, IL-8 demonstrated to promote the rate of synthesis of a pro-inflammatory types of cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-Alpha), which might contribute to the formation of a pro-tumorigenic milieu (X. Wang & Cheng, 2020). IL-8 signaling has been targeted as a potential treatment approach for breast cancer, in part because of its function in controlling the immune response and fostering inflammation. By blocking IL-8 signaling, it may be possible to reduce immune cell recruitment and suppress the creation of an inflammatory mediator's microenvironment, thereby inhibiting tumor growth and improving treatment outcomes. An inflammatory cytokine known as Interleukin-8 (IL-8) regulates the immune system and promotes the formation of a pro-inflammatory milieu in breast cancer. Within the tumour microenvironment, both cancer cells and immune cells release IL-8, which has been shown to draw neutrophils and other immune cells to the tumour places, where they help to create an inflammatory response (Fontvieille et al., 2022).

It is considered that this inflammatory response promotes tumour growth and metastasis. In addition to its involvement in immune cell recruitment, IL-8 has been demonstrated to alter the activity of immune cells such as natural killer cells and all type of T cells, as well as dampen the immune response, supporting tumor progression (X. Wang & Cheng, 2020). The previuslly published reports are available whereby different researchers have slected different SNPs like -251 A/T and 320 C/T, however, to the best of our knowledge, no published report is available currently on analysis of genetic polymorphism association of interleukin-8 (+781 C/T) in breast cancer patients. The aim of this research was elucidate relationship between environmental variables, genetic variation (IL-8, +781 C/T) polymorphism, and breast cancer in Pakistan. Firstly, the effects of environmental variables and biochemical parameters on breast cancer risk were assessed, and secondly, the IL-8 (+781 C/T) polymorphism and breast cancer relationship susceptibility was investigated.

Materials and Methods

Family history of breast cancer and corresponding treatment were queried within the questionnaire to gather pertinent familial medical data for analysis. Samples collected from hospitals in Lahore and Sargodha, samples include 100 patients and 50 healthy individuals, necessitating storage at -20°C.

Blood from breast cancer patients, along with biochemical markers and demographic data, was obtained via questionnaire with consent for future research. For DNA extraction from blood samples, a Thermo scientific kit was utilized. The SNP (+781 C/T) was genotyped via PCR, a lab method amplifying specific DNA sequences. Using a thermocycler, controlled heating and cooling separated DNA strands, with DNA polymerase and primers added to duplicate the target sequence, including specific primers for the (+781 C/T) polymorphism as shown in given Table 1. Samples, including Taq DNA polymerase, genomic DNA, PCR buffer, dNTP, Mgcl2, and primers, were centrifuged in a PCR tube and labeled before undergoing thermocycling with 30 µl of reaction mixture. Polymerase chain reaction involved denaturation at 95°C for 5 minutes, followed by 30 cycles of heating to 95°C for 1 minute, 59°C for 1 minute, and 72°C for 60 seconds, with a final extension at 72°C for 1 minute. PCR samples sorted by size via gel electrophoresis: DNA moves through agarose gel under electric

charge, smaller molecules traveling faster through the 1.5% matrix.
Data for quantitative variables presented as mean ± SD, qualitative as frequency. Independent t-test for quantitative, Chi-square for categorical, and Pearson correlation for variable correlation, analyzed using SPSS 25.0, significance set at $P < 0.05$.

Results

Frequency distribution of all demographic's values

Table 2 compares demographic characteristics of 100 breast cancer patients and 50 healthy individuals using t-test for age (mean ± SD) and chi-squared test for categorical data, with significance set at $p < .05$.

Age group and physical activity

In the control group (n=50), the mean age with SD is 29 ± 4.51, whereas the mean age with SD in the breast cancer patients (n=100) sample is 42.29 ± 8.34. P-value (.000***) denotes a significant difference in the age groups. Table 2 compares smoking history between breast cancer patients (n=100) and controls (n=50): 40 (40%) patients smoked, while 6 (12%) controls did. Significant gender group differences (p=12.29***) were graphically depicted from Table 2 results.
Physical activity levels were assessed in Table 3 among breast cancer patients (n=100) and controls (n=50): 19 (19%) patients were frequent exercisers, 31 (31%) exercised occasionally, and 50 (50%) never did, while among controls, 14 (28%) were frequent exercisers, 34 (68%) exercised occasionally, and 2 (4%) never did, with a significant gender group difference (p=32.10***).

Genotype and allele

Table 3 summarizes the frequency distribution of genotype CC, CT, and TT as well as the frequency distribution of Alleles C and T. Table 3 shows in the control group, 36 (72%) individuals had CT genotype, 14 (28%) had TT genotype, and no CC genotype. Among 100 breast cancer cases, 67 (67%) had CT genotype, 33 (33%) had TT genotype, and no CC genotype. CT genotype prevalence was highest in patients (67%) and controls (72%), graphically depicted in Fig. 5; Chi-square (x2) calculation hindered by absence of CC group (Fig. 1).
The presence of allele C 36 (36%) and T 64 (64%) in the control group; in the breast cancer patients group frequency of allele C is 67 (33.5%) and the frequency of allele T is 133 (66.5%). The occurrence of allele T is greater in both study groups. P-value (.67) indicates a there are no significant differences in allele groups (Fig. 2).

Association of age and biochemical parameters

Association of age, creatinine, CRP, and CTC on the basis of the control group and breast cancer patients were tested using T-test (Figs. 3-5). The results were concluded as mean ± standard deviation (SD). The significance of the results was measured by their *p*-values in Table 4.
Individuals in the control group (n=50) have mean age with SD 29.00±4.51 as compared to breast cancer patients (n=100) 42.29±8.34 with a P > **.000*****,** which was statistically significant. Individuals in the control group (n=50) have mean Creatinine with SD .78±.13 as compared to breast cancer patients (n=100) .77±.24 with a P > .65 which was statistically non-significant.
Individuals in the control group (n=50) have mean Anti-CCP with SD 0.60±.19 as compared to breast cancer patients (n=100) 17.64±13.30 with a P > **.000*****,** which was statistically significant (Table 4). Individuals in the control group (n=50) have mean CRP with SD .54±.25 as compared to breast cancer patients (n=100) 4.31±3.80 with a P > **.000*****,** which was statistically significant (Table 4). The results are represented graphically based on the mean values of the control and breast cancer patient groups.

Correlation among age and biochemical parameters (Creatinine, CRP, and CTC)

The Pearson formula calculated the correlation between age and biochemical parameters (Creatinine, CRP, and CTC). Age is positively correlated with CRP **(.387***)** and CTC **(.369***).** CRP is positively correlated with CTC (.270***) which represented that the value of one variable will increase with the increase of the value of other variable (Table 5).

IL-8 (+781 C/T) polymorphism was analyzed via PCR using synthesized primers, Forward: 5'-GTGGTATCACAGAGGATTATGC-3' and Reverse: 5'-CAGTCATAACTGACAACATTGATC-3', then separated on 1.5% and 2% agarose gel with ethidium bromide staining. UV analyzer documented bands, indicating TT (118 bp) and CT (118 bp, 44 bp) genotypes, with TT showing one band and CT showing two bands (Figure 6).

Discussion

A major global health concern is cancer of the breast with significant unfulfilled healthcare needs. Breast cancer's worldwide burden is inescapable as rates of incidence grow in less developed places, but a short lifespan does not have to be inescapable. Persistent and equitable gains in results from this curable disease will need deliberate and concerted efforts in all regions of the globe in the coming years. Future research to discover effective solutions, as well as continuing assessment to measure the efficacy of these efforts, is critical to reducing the present inequities (Wilkinson & Gathani, 2022).

In a study by Farbod *et al. (*2022), based on all known research, they assessed the relationship between IL-8 -251T/A and IL-18 -607C/A polymorphisms with cancer of the breast risk in this analysis. They discovered that the IL-8 (-251T/A) and IL-18 (-607C/A) polymorphisms are strongly related to an elevated risk of breast cancer in the worldwide community by aggregating all qualifying data. Our findings reveal that the IL-18 (-607C/A) and IL-8 (-251T/A) polymorphisms are strongly related to an elevated risk of breast cancer. Our findings further suggest that the IL-8 (-251T/A) polymorphism contributes to the occurrence of cancer of the breast in Africans. To corroborate our findings, larger sample sizes and additional ethnic groupings are required in future investigations (Farbod et al., 2022).

IL-8 present in humans, known to the world as a chemotactic factor of neutrophil, has considerable promise as a predictive and prognostic biomarker in a variety of inflammatory and malignant conditions. The acquisition of neutrophils and other immune system cells needs to spread the disease site. IL-8 has 4 exons, a distal promoter region, and an overall length of 5191 bp. It is located on chromosomal 4q13 and q21. Furthermore, human IL-18, an IL-1 family member, initially emerged as a protein that promotes interferon, or IFN, generation. It is known as inflammatory mediator's chemokine that performs an important role in the beginning, regulation, and ongoing maintenance of the gut immune response (Farbod et al., 2022).

The analyzed genotype pattern among the control (n=50) and cancer of the breast patient (n=100) groups reveals significant tendencies. The CT genotype was most common in the control group (72%, n=36), followed by the TT genotype (28%, n=14), while the CC genotype was missing. Similarly, the CT genotype predominated (67%, n=67) among breast cancer patients, with the TT genotype found in 33% (n=33) and no cases of the CC genotype. Chi-square (2) calculation was impossible due to the lack of the CC genotype. The constant incidence of CT genotype between the two populations needs additional investigation, perhaps indicating a link between this genotype and breast cancer risk. However, more research is needed to determine the importance of these results and to establish any possible genetic links. C and T allele frequencies were determined in the unaffected and breast cancer patients respectively. While the T allele was dominant in both groups, no significant variations were seen (Bilal et al., 2024).

The study included a control group (n=50) with a mean Creatinine of.78.13 and breast cancer patients (n=100) with.77.24, generating a non-significant P >.65. This suggests that there is no discernible variation in Creatinine levels across the groups. The data show that creatinine may not be a differentiating factor in this circumstance. Further research into different biomarkers might give further information about possible clinical or prognostic

signs of breast cancer (Bilal et al., 2021&2024).
The study found a substantial difference in Anti-CCP levels among the control class and breast cancer patients. This significant finding suggests that Anti-CCP might be used to identify breast cancer patients. These results highlight the necessity of researching the function of Anti-CCP in the development of cancer of the breast to help in early identification and enhanced therapy techniques. Another statistically significant finding emphasizes CRP's potential as a useful diagnostic for detecting cancer in breast individuals. Additional studies into the relationship between CRP and cancer in women may yield insights into its involvement in disease development as well as its value in diagnostic and predictive methods (Bilal et al., 2021&2024).
It is well acknowledged that cancer of the breast is a complex illness and that disease pathogenesis may typically be aided by a single dominant alteration leading to the development of genes associated with vulnerability. It is critical to apprehend the specific genetic criminals who are accountable for the functional alterations of susceptibility genes. At least 1% of DNA variations in sequence exist. Individual nucleotide changes induce mutations in a population. These kinds of mutations comprise the transversion, insertion, or deletion of a single base and are considered to play a role in altering protein function and raising vulnerability to disease in humans. Previous research found that aggressive breast cancer cells expressed a high level of IL-8 in both in vivo and in vitro investigations (Zhang, Han, & Sun, 2017).
According to certain research, the IL-8 251A/T, 781 CT/ haplotype can affect the IL-8 expression of proteins at the transcriptional phase. Current research has linked IL-8 +781C/T to malignancies such as osteosarcoma, glioma, and ovarian cancer, hepatic cell carcinoma, and mouth cancer (Zhang et al., 2017).
In this current study, a comparison of demographic features between cancerous breast patients (n=100) and healthy persons (n=50) from a sample of 150 people was performed. A t-test for mean and standard deviation was used to analyze age, which was measured in years. A chi-squared test was used to examine categorical characteristics. Significance at p0.05 was used to evaluate significant differences between classes. There was a significant difference in the age of patients and healthy individuals. Another history of smoking in this study was performed on 100 breast cancer patients and 50 control subjects. Gender disparities are highlighted by a highly significant p-value (12.29***). This demonstrates a significant link between smoking history and breast cancer, highlighting the significance of this factor in the incidence of the disease.
The assessment of exercise between breast cancer patients (n=100) and the control group (n=50) indicated significant patterns. In the individual patient's sample, 50% said they never engaged in physical activities, whereas 19% and 31% said they did so frequently and sometimes, respectively. In the control group, however, 68% indicated sometimes physical activity, 28% engaged regularly, and only 4% never engaged. The significant p-value (p0.001) suggests an important gender discrepancy. These findings highlight the need for focused interventions to increase activity levels, especially among breast cancer patients, since it appears as a significant factor that may have health and well-being consequences. More study is needed to investigate the complicated relationship between exercise, illness, and gender (Posner, Barrington, Brier, & Datta-Mannan, 2019).

Conclusions

This comprehensive research and results show that the CT genotype was much more common in breast cancer patients with the IL-8 +781 C/T polymorphism. Individuals with the TT genotype of IL-8 +781 C/T were shown to be more susceptible to breast cancer, indicating a possible link between this genetic variation and the chance of acquiring the illness. While our findings give significant insight into the genetic background of breast cancer, it is critical to emphasize the need for more substantial research to confirm our findings. Pearson's method was also used to calculate correlations between age and biochemical markers (creatinine, CRP, and CTC). The findings revealed a favorable relationship between age and CRP (r = 0.387***) as well as CTC (r = 0.369***). Notably, CRP correlated positively with CTC (r = 0.270***), indicating a reciprocal impact between both variables. According to the findings of this extensive study, the CT genotype was substantially more prevalent in breast cancer patients with the IL-8 +781 C/T polymorphism. To establish the robustness and generalizability

of these data, larger sample numbers, various populations, and complete molecular investigations are necessary. The potential consequences of these results might include emphasizing the importance of ongoing study into the delicate relationship between genetic variables and carcinoma of the breast risk.

Acknowledgement
We express our sincere gratitude to the administration committee of INMOLE Cancer Hospital, Lahore, and District Head Quarter Hospital, Sargodha, for their invaluable insights and assistance in sample collection, which significantly enhanced the quality of this research. We also extend our heartfelt thanks to the University of Sargodha, Pakistan, for providing state-of-the-art facilities that made this study possible. Each contribution has had a substantial impact on the outcomes of this research.

Funding
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest
The authors confirm no conflict of interest.

References
Farbod, M., Dastgheib, S. A., Asadian, F., Karimi-Zarchi, M., Sayad, S., Barahman, M., . . . Neamatzadeh, H. (2022). Association of IL-8 -251T>A and IL-18 -607C>A polymorphisms with susceptibility to breast cancer - a meta-analysis. Klin Onkol, 35(3), 181-189. doi:10.48095/ccko2022181

Fontvieille, E., His, M., Biessy, C., Navionis, A. S., Torres-Mejía, G., Ángeles-Llerenas, A., . . . Rinaldi, S. (2022). Inflammatory biomarkers and risk of breast cancer among young women in Latin America: a case-control study. BMC Cancer, 22(1), 877. doi:10.1186/s12885-022-09975-6

Giaquinto, A. N., Sung, H., Miller, K. D., Kramer, J. L., Newman, L. A., Minihan, A., . . . Siegel, R. L. (2022). Breast Cancer Statistics, 2022. CA Cancer J Clin, 72(6), 524-541. doi:10.3322/caac.21754

Bilal, A., Tanvir, F., Ahmad, S., Kanwal, N., Zulfiqar, H., & Ishaq, R. (2024[a]). Pharmacokinetic Properties of Bioactive Compounds of Aloe vera against Pregnancy-Associated Plasma Protein A (PAPP-A) inducing Triple-Negative Breast Cancer. Kurdish Studies, 12(5), 157-168.

Bilal, A., Tanvir, F., Ahmad, S., Azam, A. R., Qasim, M., Zafar, H., & Tanvir, F. (2024[b]). Therapeutical evaluation of bioactive compounds of Nigella sativa for HER2-positive breast cancer treatment. Journal of Population Therapeutics & Clinical Pharmacology, 31(9), 3149-3164.

Hou, N., Hong, S., Wang, W., Olopade, O. I., Dignam, J. J., & Huo, D. (2013). Hormone replacement therapy and breast cancer: heterogeneous risks by race, weight, and breast density. J Natl Cancer Inst, 105(18), 1365-1372. doi:10.1093/jnci/djt207

Jin, Z., Zhao, Y., Sun, Y., Zhang, B., Wang, H., Wu, Y., . . . Rao, Z. (2020). Structural basis for the inhibition of SARS-CoV-2 main protease by antineoplastic drug carmofur. Nat Struct Mol Biol, 27(6), 529-532. doi:10.1038/s41594-020-0440-6

Liu, J., Li, Y., Li, Q., Liang, D., Wang, Q., & Liu, Q. (2021). Biomarkers of response to camrelizumab combined with apatinib: an analysis from a phase II trial in advanced triple-negative breast cancer patients. Breast Cancer Res Treat, 186(3), 687-697. doi:10.1007/s10549-021-06128-4

Bilal, A., Naveed, N., & Haider, M. (2021). A brief note on cancer and its treatment. Occup Med Health Aff, 9(7), 1-3.

Bilal, A., Tanvir, F., Ahmad, S., Shah, S. H. A., Ahmad, H. A., & Kanwal, N. (2024[c]). Pre-clinical study of the bioactive compound Asiaticoside against the proteins inducing human mammary carcinoma using molecular docking and ADME analysis. Remittances Review, 9(2), 3543-3576.

Peng, J., Madduri, S., Clontz, A. D., & Stewart, D. A. (2023). Clinical trial-identified inflammatory biomarkers in breast and pancreatic cancers. Front Endocrinol (Lausanne), 14, 1106520. doi:10.3389/fendo.2023.1106520

Noor, A., Bilal, A., & Ali, U. (2024). Towards personalized cancer care: A report of CRISPR-Cas9 applications in targeted therapies and precision medicine. Journal of Health and Rehabilitation Research, 4(2), 1375-1380.

Posner, J., Barrington, P., Brier, T., & Datta-Mannan, A. (2019). Monoclonal Antibodies: Past, Present and Future. Handb Exp Pharmacol, 260, 81-141. doi:10.1007/164_2019_323

Ramirez, A. G., Parma, D. L., Muñoz, E., Mendoza, K. D., Harb, C., Holden, A. E. C., & Wargovich, M. (2017). An anti-inflammatory dietary intervention to reduce breast cancer recurrence risk: Study design and baseline data. Contemp Clin Trials, 57, 1-7. doi:10.1016/j.cct.2017.03.009

Rogers, L. Q., Fogleman, A., Trammell, R., Hopkins-Price, P., Spenner, A., Vicari, S., . . . Verhulst, S. (2015). Inflammation and psychosocial factors mediate exercise effects on sleep quality in breast cancer survivors: pilot randomized controlled trial. Psychooncology, 24(3), 302-310. doi:10.1002/pon.3594

Bilal, A. (2021). Clinical diagnosis and treatment of absence seizures: Case study. MAR Ophthalmology, 2(1).

Tiainen, L., Hämäläinen, M., Luukkaala, T., Tanner, M., Lahdenperä, O., Vihinen, P., . . . Kellokumpu-Lehtinen, P. L. (2019). Low Plasma IL-8 Levels During Chemotherapy Are Predictive of Excellent Long-Term Survival in Metastatic Breast Cancer. Clin Breast Cancer, 19(4), e522-e533. doi:10.1016/j.clbc.2019.03.006

Wang, Y. C., Wang, Z. H., Yen, J. H., Shen, Y. C., Shen, T. C., Chang, W. S., . . . Tsai, C. W. (2022). The Contribution of Interleukin-8 Rs4073 Genotypes to Triple Negative Breast Cancer Risk in Taiwan. Anticancer Res, 42(8), 3799-3806. doi:10.21873/anticanres.15870

Wilkinson, L., & Gathani, T. (2022). Understanding breast cancer as a global health concern. Br J Radiol, 95(1130), 20211033. doi:10.1259/bjr.20211033

Yu, L. Y., Tang, J., Zhang, C. M., Zeng, W. J., Yan, H., Li, M. P., & Chen, X. P. (2017). New Immunotherapy Strategies in Breast Cancer. Int J Environ Res Public Health, 14(1). doi:10.3390/ijerph14010068

Zhang, J., Han, X., & Sun, S. (2017). IL-8 -251A/T and +781C/T polymorphisms were associated with risk of breast cancer in a Chinese population. Int J Clin Exp Pathol, 10(7), 7443-7450.

Zhu, J., & Paul, W. E. (2008). CD4 T cells: fates, functions, and faults. Blood, 112(5), 1557-1569. doi:10.1182/blood-2008-05-078154

Zhu, Z. Y., Xue, J. X., Yu, L. X., Bian, W. H., Zhang, Y. F., Sohn, K. C., . . . Yao, C. (2018). Reducing postsurgical exudate in breast cancer patients by using San Huang decoction to ameliorate inflammatory status: a prospective clinical trial. Curr Oncol, 25(6), e507-e515. doi:10.3747/co.25.4108