

## The Role of Physical Activity on Some Biochemical Parameters in Cancer Treatment

Egemen DERE<sup>1</sup>

(Geliş Tarihi/Received: 20.09.2023; Kabul Tarihi/Accepted: 07.12.2023)

### Abstract

Cancer poses a serious public health problem. Recent studies underscore the crucial role of exercise in enhancing the quality of life for cancer patients, both during and after treatment, and its potential positive impact on treatment outcomes. This article assesses the importance of physical activity in the context of cancer, drawing on current data.

Cancer treatment is a long-term process that includes different methods and strategies. Crafting a treatment plan hinges on factors such as the patient's age, overall health, specific cancer type, and its staging. The main methods of cancer treatment include chemotherapy, radiotherapy, immunotherapy, surgical procedures, targeted therapies, hormone therapy and stem cell transplantation. One of the ways to reduce the side effects that occur in patients treated with one or more of these methods is to do aerobic and resistance exercises.

Research emphasizes the increasing importance of physical activity in cancer treatment. This period is characterized by increased emotional stress. Regular exercise has proven benefits. Exercise stimulates the release of endorphins, reduces depression, anxiety and promotes better sleep quality. Furthermore, it serves to alleviate side effects such as fatigue, muscle loss, weight gain, and diminished bone density. Additionally, regular exercise contributes to fortifying the immune system, enhancing resistance against infections. Notably, a research highlights that women with breast cancer exhibit a reduced risk of cancer recurrence when they incorporate exercise into their lives.

Exercise in cancer treatment exerts a significant influence on enzyme activities, potentially leading to alterations in metabolic processes. Enzyme activities may either rise or fall based on their impact on metabolism. Notably, exercise has been shown to boost the activity of antioxidant enzymes while simultaneously diminishing oxidative stress. This effect holds particular importance when considering cancer treatment, as oxidative stress is known to facilitate the growth and dissemination of cancer cells.

In conclusion, it can be said that the importance of exercising during and after cancer treatment is increasingly understood. However, since each patient's cancer is unique, physical activities need to be individually tailored and monitored by experts.

**Keywords:** Aerobic exercise, cancer treatment, physical activity

### Kanser Tedavisinde Bazı Biyokimyasal Parametreler Üzerine Fiziksel Aktivitenin Rolü

#### Özet

Kanser ciddi bir halk sağlığı sorunu oluşturmaktadır. Son araştırmalar, kanser hastalarının hem tedavi sırasında hem de sonrasında yaşam kalitesini artırmada egzersizin önemli rolünün ve tedavi sonuçları üzerindeki potansiyel olumlu etkisinin altını çiziyor. Bu makale, güncel verilerden yararlanarak, kanser bağlamında fiziksel aktivitenin önemini değerlendirmektedir.

Kanser tedavisi farklı yöntem ve stratejileri içeren uzun vadeli bir süreçtir. Bir tedavi planı hazırlamak hastanın yaşı, genel sağlık durumu, spesifik kanser türü ve evrelemesi gibi faktörlere bağlıdır. Kanser tedavisinin ana yöntemleri arasında kemoterapi, radyoterapi, immünoterapi, cerrahi prosedürler, hedefe yönelik tedaviler, hormon tedavisi ve kök hücre nakli yer alır. Bu yöntemlerden bir veya birkaçı ile tedavi edilen hastalarda ortaya çıkan yan etkileri azaltmanın yollarından biri aerobik ve direnç egzersizleri yapmaktır.

Araştırmalar kanser tedavisinde fiziksel aktivitenin artan önemini vurgulamaktadır. Bu dönem artan duygusal stres ile karakterizedir. Düzenli egzersizin kanıtlanmış faydaları vardır. Egzersiz, endorfin salınımını uyarır, depresyonu, kaygıyı azaltır ve daha iyi uyku kalitesini artırır. Ayrıca yorgunluk, kas kaybı, kilo alımı ve kemik yoğunluğunun azalması gibi yan etkilerin hafifletilmesine de hizmet eder. Ayrıca düzenli egzersiz bağışıklık sisteminin güçlendirilmesine, enfeksiyonlara karşı direncin artmasına katkıda bulunur. Özellikle, bir araştırma meme kanseri olan kadınların egzersizli yaşamlarına dahil ettiklerinde kanserin tekrarlama riskinin azaldığını vurgulamaktadır.

Kanser tedavisinde egzersiz, enzim aktiviteleri üzerinde önemli bir etkiye sahiptir ve potansiyel olarak metabolik süreçlerde değişikliklere yol açmaktadır. Enzim aktiviteleri metabolizma üzerindeki etkilerine bağlı olarak artabilir veya azalabilir. Özellikle

<sup>1</sup> Doç. Dr., Department of Biology, Art and Science Faculty, Bursa Uludag University, 16059, Bursa-Turkey  
ORCID: 0000-0001-9572-1051; e-posta: edere@uludag.edu.tr

egzersizin antioksidan enzimlerin aktivitesini arttırırken aynı zamanda oksidatif stresi azalttıđı gösterilmiřtir. Oksidatif stresin kanser hücrelerinin büyümesini ve yayılmasını kolaylařtırdıđı bilindiđinden, kanser tedavisi düşünöldüđünde bu etki özel bir öneme sahiptir.

Sonuçta, kanser tedavisi sırasında ve sonrasında egzersiz yapmanın öneminin giderek daha fazla anlařıldıđı söylenebilir. Ancak her hastanın kanseri kendine özel olduđu için yapılacak fiziksel aktivitelerin bireysel olarak planlanması ve uzmanlar tarafından takip edilmesi gerekmektedir.

**Anahtar kelimeler:** Aerobik egzersiz, kanser tedavisi, fiziksel aktivite

## Introduction

For many individuals who learn they have cancer, this disease can pose a life-threatening challenge. The treatment process is prolonged and exhausting, requiring patients to contend not only with the cancer itself but also with the side effects arising during the treatment (Hauth et al. 2021). In this meaning, providing social support to cancer patients is crucial (Roscoe et al. 2022). The American Society of Clinical Oncology (ASCO) has released a research indicating that personalized aerobic exercises conducted during cancer treatment yield positive effects (Ligibel et al. 2022). In research involving patients with prostate, breast, lung, and colorectal cancer, it has been suggested that there is a reduction in tiredness, weakness, and significant improvements in other side effects during treatment (Ligibel et al. 2022). Other researchers have demonstrated exercise enhances survival by regulating circulating hormones (de Roon et al. 2018; Chang et al. 2020). Individuals diagnosed with cancer grapple with emotional issues such as depression, anxiety, and stress. Engaging in physical activities during and after treatment boosts the release of neurotransmitters, contributing to an enhancement in the chemical balance of the brain. One study particularly highlighted the potent impact of physical activity on dopamine (Marques et al. 2021). Consistently engaging in aerobic exercises not only enhances the wellbeing of cancer patients but also improves their overall quality of life. Furthermore, it has been proposed that incorporating exercise during neoadjuvant and adjuvant therapy enhances the effectiveness of cancer treatments (Misiag et al. 2022; Yang et al. 2021). Several studies indicate that consistent aerobic exercises may mitigate the growth and dissemination of cancer cells. Exercise plays a role in fortifying the immune system and enhancing the activity of leukocytes that combat cancer cells. Therefore, engaging in aerobic exercise during cancer treatment not only amplifies the response to therapy but also elevates the overall survival rate. Another study suggested that vigorous training prevents the proliferation and metastasis of cancer cells (Wang and Zhou 2021; Pollán et al 2020; Hayes et al. 2018; Dethlefsen et al. 2017). While research has been made to elucidate the significance and benefits of exercise in the battle against cancer, the complete biochemical foundations remain yet to be fully revealed. Nonetheless, the importance of controlled exercise during cancer treatment has been underscored (Zhu et al., 2022). Additionally, aerobic exercise has been identified as a preventive measure against metastasis. Zerhouni and Piskounova (2022) have highlighted the significance of metabolic plasticity in metastasis and elucidated the connection between metabolic reprogramming and the Mammalian Target of Rapamycin (mTOR) signaling pathway, a serine/threonine kinase belonging to the Phosphatidylinositol 3-kinase (PI3K) "related protein kinase family".

In studies conducted until 2023, it has been observed that in patients undergoing neoadjuvant or adjuvant therapy, resistance exercise or aerobic exercise results in a moderate improvement in maximum oxygen consumption (VO<sub>2</sub>max) (Wiestad et al., 2020; Yousaf and Marwat, 2022). The conjecture is that physical activity may influence tumor biology through alterations in circulating proteins RNA molecules, and metabolites (Metcalfé et al., 2021)

This article aims to provide information on how patients can enhance both their physical and mental well-being during the cancer treatment process by engaging in a regular exercise program. It emphasizes that through such activities, individuals may alleviate side effects like fatigue, depression, and sleep problems, ultimately improving their quality of life while combating cancer. The article underscores the positive contribution of physical activities undertaken during the treatment process.

### **What is Aerobic Exercise?**

Aerobic exercises are a combination of low-intensity and regular rhythmic movements, usually accompanied by a musical accompaniment. These physical activities refer to exercise programs designed to increase endurance and promote fat burning. Aerobic exercises include activities such as walking, jogging, cycling, swimming, dancing, aerobics classes, zumba. Such activities; increases heart rate, accelerates blood circulation, lowers blood pressure, increases respiratory rate and depth. It encourages muscle work and energy expenditure in the body. It keeps cholesterol levels under control.

It reduces stress and improves overall physical and mental health (Permadi 2019).

### **What is Resistance Exercise?**

Resistance exercise is a type of exercise performed by applying resistance to the muscles we use. These exercises are usually performed using tools or equipment that provide resistance, such as weights, elastic bands, swing arms, or body weight. We can count all of the trainings using weights in this class. Resistance exercises are used to increase muscle mass, improve strength and endurance, increase bone density, improve body composition and raise overall fitness levels. It is also widely preferred in the rehabilitation process (Zhao et al. 2022).

### **Benefits of Regular Aerobic and/or Resistance Exercise During Cancer Treatment**

The lack or decrease of physical activity causes the energy balance to be disrupted and excessive fat accumulation in the tissues, especially obesity. This is one of the causes of many chronic diseases. It is noteworthy that many patients with breast cancer do not exercise at all (Huneidi et al. 2018). Cancer treatment can sometimes affect heart health. In particular, some chemotherapy drugs can damage the heart muscle. Exercise can improve heart function and strengthen the circulatory system by supporting cardiovascular health. It has been shown that muscles act as an endocrine structure and regulate metabolism during regular exercises (Severinsen and Petersen. 2020). The primary mechanisms through which exercise proves advantageous in the prevention and treatment of cancer include inducing apoptosis, inhibiting the proliferation of cancer cells, and regulating cancer metabolism and immunity. Figure 1 illustrates some of these key mechanisms (Wang and Zhou 2021). Engaging in a regular exercise program during cancer treatment is an effective method for improving sleep, particularly alleviating feelings of fatigue, enhancing overall quality of life, reducing stress, regaining muscle strength, and mitigating various potential side effects. Research indicates that aerobic or

resistance exercises during cancer treatment lead to modest yet statistically significant improvements (Hilfiker et al., 2018; Rasmussen et al. 2020).

However, engaging in excessively intense single-session exercises may increase the level of generated free radicals, surpassing the capacity of the antioxidant defense system and leading to oxidative stress. Excessive radical production can induce changes in the DNA structure, potentially causing alterations in the genetic makeup and triggering the formation of cancer. Therefore, to reduce the risk of cancer, it is recommended to participate in short-duration, moderate-intensity physical activities. In this context, a personalized exercise plan tailored to the individual should be developed. Regular exercise is noted to preserve telomere structure, prevent telomere shortening, and reduce the risk of cancer (Haupt et al. 2022).

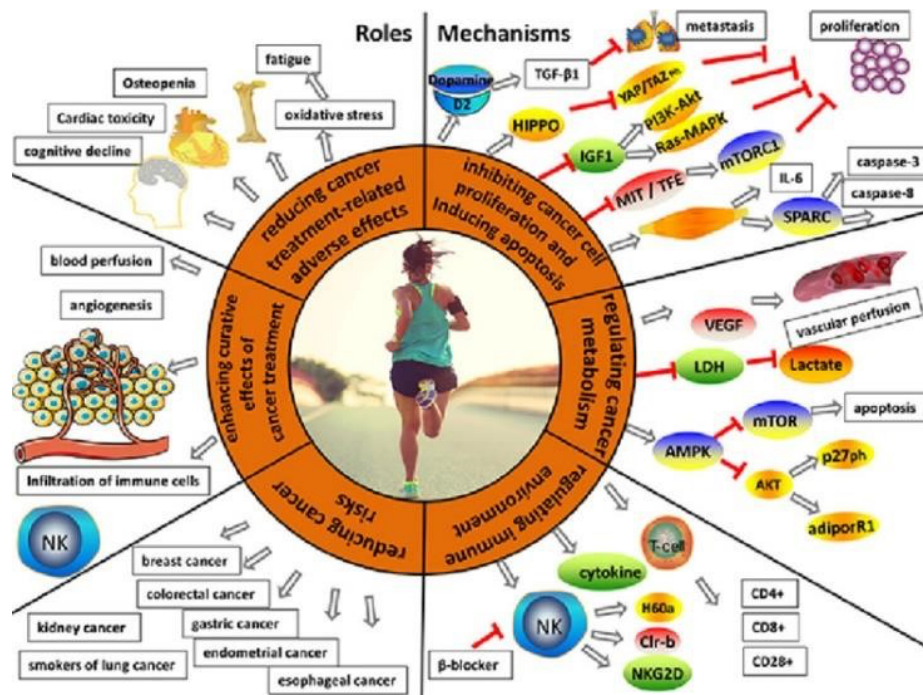


Figure 1. Main mechanisms by which exercise benefits in preventing and treating cancer (Wang and Zhou 2021).

**Improving mental health:** Following aerobic exercises, positive developments in both cortical and subcortical areas of the brain have been reported (Chen et al. 2020). Individuals who engage in regular aerobic exercise experience an increase in the synthesis of serotonin, a neurotransmitter known as the happiness hormone. Serotonin not only regulates the sleep pattern in the brain, promoting a healthier sleep, but also contributes to the regulation of the digestive system due to its abundance in gastrointestinal system cells (Abdulrasool et al. 2020). In their review study, Yang et al. (2021) suggested that physical activity can enhance sleep quality in breast cancer patients. It has been demonstrated that relaxation exercises improve sleep quality in breast cancer patients undergoing chemotherapy (Nazik et al., 2014). Additionally, Baran (2021) proposed

that exercise could potentially correct the loss of sensory perception in the arm experienced by breast cancer patients undergoing treatment.

**Managing side effects:** Exercise enhances energy levels, mitigates fatigue, improves overall quality of life by boosting muscle strength and endurance, and aids in managing side effects. In breast cancer patients undergoing chemotherapy or radiotherapy, as well as in colorectal and lung cancer patients undergoing chemotherapy, those with prostate cancer undergoing radiation therapy, and individuals with hematological cancers, engaging in exercise during treatment has been reported to contribute to a moderate reduction in fatigue (Shao et al. 2022; Yang et al. 2022). In body muscle strength; it has been suggested that it causes improvements in breast cancer patients, causes significant improvements in men with prostate cancer, and has a lesser effect in some other types of cancer. In an evaluation of studies examining the effect of exercise on strength in men with prostate cancer, it was suggested that there is a significant relationship between resistance exercise and changes in upper body strength (Piroux et al. 2020). Lymphedema is one of the side effects that occur after drugs or surgical interventions in many pathophysiological cancer patients. Lymphedema causes serious problems, especially in the arms.

Physical activity has been shown to be very important in the treatment of lymphedema (Basha et al. 2022).

**Reducing the risk of recurrence:** Regular physical activity has been associated with a reduced risk of cancer recurrence and increased survival rates for several types of cancer, including breast, colorectal, prostate, and ovarian cancers (Cormie et al. 2017). Exercise helps inhibit tumor growth, reduce inflammation, and improve hormonal balance. All of these contribute to reducing the risk of cancer recurrence. In one study, it was shown to completely prevent cancer recurrence in patients rather than delay it (Morishita et al. 2020; Brown et al. 2023).

**Operation:** Analyses were undertaken to assess the impact of preoperative exercise on postoperative complications and other outcomes in patients undergoing surgery for gastrointestinal cancers (Lee and Oh, 2021) and genitourinary cancers (Bessa et al., 2021; Wang and Zhou, 2021). It has been reported that engaging in preoperative exercise, particularly in patients with non-small cell lung cancer, leads to a reduction in postoperative hospital stay (Avancini et al., 2020; Onerup, 2021). If breast cancer patients engage in exercise following their surgeries, it has been demonstrated that insulin-like growth factor-1 (IGF-1), interleukin-6 (IL-6), C-reactive protein (CRP), interleukin-10 (IL-10), and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) levels can be significantly affected, as evidenced by Zhou et al. (2022). This effect plays a substantial role in preventing cancer recurrence and promoting healing, particularly through the reduction of TNF- $\alpha$  levels. It has been proposed that engaging in physical activity may contribute to the prevention of approximately 15% of colon cancers (Oruç and Kaplan, 2019). The protective effect of exercise against colon cancer is attributed to increased prostaglandin synthesis, resulting in the cessation of colon cell proliferation, reduced bile acid

concentration, and decreased circulating insulin and glucose levels during activity. In a study conducted by Kim et al. (2020), it was found that IGF-1, soluble tumor necrosis factor receptor-2 (sTNFR-2), and interleukin-8 (IL-8) levels are associated with an elevated risk of colorectal cancer, especially among individuals who regularly engage in physical activity and adhere to anti-inflammatory dietary patterns. The study indicated that IGF-1 tended to exhibit a significant inverse relationship with sTNFR-2 and IL-8. Consequently, the researchers suggested that physical activity exerts cancer-preventive effects throughout the emergence and progression of colorectal cancer

### **Exercise in Individuals Living With Advanced Cancer**

Studies on the significance of exercise in advanced cancer patients are relatively scarce in the literature. Nonetheless, it is proposed that exercise can be beneficial at any stage (Torregrosa et al., 2022). The performance of exercise by patients with bone metastases has been suggested to mitigate severe side effects associated with the disease. Additionally, engaging in exercise by patients with advanced lung cancer has been demonstrated to alleviate certain disease-specific side effects, leading to a noteworthy improvement in the patient's condition (Capozzi et al., 2021). Electromyostimulation (EMS) has shown considerable benefits for individuals with advanced cancer (Schink et al., 2018).

### **The Effect of Exercise on Some Biochemical Parameters**

Exercise induces the synthesis of cytokines in skeletal muscles, which are crucial for intracellular and intercellular communication and play a role in immune system regulation. Cytokines contribute to both anabolic and catabolic processes in skeletal muscle (Lee and Margolin, 2011). Numerous myokines are present in muscles, with new ones continuously being discovered. Particularly after resistance exercises, there is an upsurge in cytokines/myokines in skeletal muscle (Severinsen and Petersen, 2020).

The impact of exercise on cytokines can be intricate and varies based on factors such as the type and intensity duration of exercise, and the individual's overall health. For instance, moderate aerobic exercise can decrease pro-inflammatory cytokine levels while increasing anti-inflammatory cytokine release (Docherty et al., 2022). Cytokines act as immunomodulatory agents, operating through autocrine, paracrine, and endocrine signaling, preventing the growth of cancer cells and promoting apoptosis, thus hindering cancer cell proliferation.

Key myokines in muscles include IL-6, which regulates immune and inflammatory responses; Interleukin-15 (IL15), playing a potential role in the growth and repair of skeletal muscle fibers;

Fibroblast Growth Factor-21 (FGF21), which has a fat-reducing effect; Brain-Derived Neurotrophic Factor (BDNF), crucial for neuronal development and healthy functioning, and Irisin. Studies by Lee and Jun (2019) identified some myokines (IL-6, IL-15, BDNF, SPARCO, FGF21, Decorin, Myonectin, Myostatin, Irisin) and the metabolic pathways they affect.

In a study on pancreatic cancer patients, interleukin-10 (IL10), C-X-C motif ligand-1 (CXCL-1), and CC motif chemokine ligand-4 (CCL4) were identified as myokines released from active skeletal muscle (Schwappacher et al., 2021).

Exercise helps combat insulin resistance induced by certain cancer treatment drugs, affecting prostate cancer progression by reducing IGF-1, increasing adiponectin levels, and regulating circulating insulin. IL-6 has been shown to promote cell proliferation and inhibit apoptosis in vitro in prostate cancer cells (Deb et al., 2019). Personalized exercise programs have been suggested to correct insulin resistance during breast cancer treatment (Iwase, 2021).

Studies on the effects of aerobic exercise in breast cancer mice revealed a decrease in chemokines CCL2 and CCL5 and their relative receptors, indicating a positive impact on breast cancer (Esmailiyan et al., 2022). Resistance exercises moderately reduced body fat percentage in prostate cancer patients, leading to decreased low-density lipoprotein (LDL) in fatty acids (Teixeira et al., 2020).

Regular physical activity plays a role in cancer prevention by suppressing pathways such as mTOR, Hippo signaling pathway (YAP-TAZ), and Akt, which are pivotal in proliferation (Wang and Zhou, 2021; Chen et al., 2022).

Adiposity and adipokines, released due to physical activity, act as hormone and cytokine-like mediators, potentially serving as a weapon against cancer and metastasis. Physical activity stimulates metabolism, reducing adipose tissue volume, thereby modulating adipokine secretion, immune functions, and inflammatory state, ultimately reducing the risk of carcinogenesis, blocking metastasis, and increasing survival (Perego et al., 2021).

Mitochondrial number and activity are regulated by Peroxisome Proliferator-Activating Receptor

Gamma Coactivator 1-alpha (PGC-1 $\alpha$ ). Aerobic exercises induce PGC-1 $\alpha$  expression, increasing mitochondrial activity and energy molecule production. Irisin enhances PGC-1 $\alpha$  activation, allowing fatty acids to participate in energy metabolism, thereby supporting metabolism. A sedentary lifestyle may decrease PGC1- $\alpha$  levels in muscles (Bozkurt, 2021).

Caspase proteases, essential for apoptosis initiation and maintenance, are categorized as initiator caspases (caspase-2, -8, -9, and -10) and executioner caspases (caspase-3, -6, and -7) (Boice and Bouchier-Hayes, 2020). Aerobic exercise has been demonstrated to have a protective effect on apoptosis, reducing caspase-9, caspase-3, and Bax to Bcl-2 levels in heart tissue (Pahlavani and Veisi, 2018).

### **Role of Physical Activity on Anti-Inflammation and Immune System**

Inflammation exhibits protective properties against breast cancer by increasing cell division, especially in breast tissue, through the stimulation of Insulin-like Growth Factor-1 (IGF-1). This process promotes cell proliferation, reduces the death of cancerous cells, and acts as a mitogen. Regular exercise plays a role in



reducing the risk of various cancers, particularly breast cancer, by increasing the level of Insulinlike Growth Factor Binding Protein 3 (IGFBP-3) and decreasing the level of IGF-1 in the blood. Consequently, inflammation is reduced.

Studies suggest that regular exercise during cancer treatment leads to a decrease in CorticotropinReleasing Factor (CRF), a significant reduction in Tumor Necrosis Factor- $\alpha$  (TNF- $\alpha$ ), C-reactive protein (CRP), interleukin-8 (IL-8), and IL-6, along with an increase in Natural Killer (NK) cell levels (AlMhanna et al., 2022). NK cells, part of the innate immune system, play a crucial role in preventing cancer metastasis by detecting and destroying potentially cancerous cells. This helps in controlling cancer cells and supports the immune system in the fight against cancer (Zheng et al., 2022).

The immune system is vital in the battle against cancer, especially considering its weakening during cancer treatment. Exercise contributes to increased activation of immune cells and improved immune function, reducing the risk of infection and supporting the healing process. In essence, regular physical exercise acts as a modulator of the immune system (da Silveira et al., 2021). It's essential to note from another study that the positive effects of physical activity in breast cancer patients persisted for a few months after exercise cessation but gradually diminished (Goldschmidt et al., 2023). Therefore, it is recommended not to abandon exercises during this period.

Furthermore, one study investigated how physical activity influences predictors of a successful T cell response against immunogenic cancer cells (Emery et al., 2022).

### **The Effect of Exercise on Energy Balance and Hormones**

During cancer treatment, the metabolic rate often decreases. Exercise plays a crucial role in regulating energy balance by increasing energy expenditure, which is essential for weight control and maintaining a healthy body composition. The myokines IL-15 and FGF-21, elevated in muscles after regular exercise, along with the peptide hormone irisin secreted from adipose and muscle tissue, enhance energy expenditure by facilitating the conversion of white adipose tissue into brown adipose tissue. Patients with breast cancer have been found to exhibit very low levels of irisin, suggesting its potential use as a biomarker. Increasing irisin levels has shown positive effects on tumor cells (Moon and Mantzoros, 2014).

Exercise also regulates the release of stress hormones such as cortisol and adrenaline, providing relief from the stress associated with cancer treatment. Physical activity has significant effects on sex hormones, suppressing tumor cells in patients with breast cancer (Swain et al., 2022). Additionally, exercise increases the release of natural pain-relieving hormones called endorphins in the brain, helping to alleviate pain and discomfort during cancer treatment (Abdulrasool et al., 2020).

The peptide hormone leptin, produced by fat cells, exhibits endocrine, autocrine, and paracrine effects, preventing apoptosis and promoting tumor formation, growth, and even metastasis (Nuri et al., 2016). Regular

exercises have been shown to decrease leptin levels and increase ghrelin levels in patients with colorectal cancer (Faris et al., 2022).

Furthermore, it has been demonstrated that moderate-intensity aerobic training leads to an improvement in IGF-1 levels and functional capacity in the elderly. Exercise increases the release of growth hormone, contributing to cell growth, recovery, and regeneration processes (Sundari and Arsani, 2022).

### **As a Result, Exercise in Cancer Treatment**

Aerobic or resistance exercise during cancer treatment has demonstrated various benefits, including the reduction of side effects such as fatigue and mood disorders. It is particularly beneficial in maintaining strength, especially for men undergoing treatment for prostate cancer. The incorporation of exercise into cancer treatment has been shown to enhance fitness and functional status in patients. The protective mechanisms of exercise against various types of cancer involve factors such as decreased body fat mass, immune system stimulation against tumors, increased antioxidant levels, and genetic factors (Zhu et al., 2022).

Physical activity induces several positive changes, including lower blood glucose and insulin levels, increased corticosteroid hormones, elevated testosterone levels for enhanced body resistance, and heightened cytokine levels that play a role in inflammation and immune responses. Exercise also amplifies the number of insulin receptors in cancer-fighting T cells, stimulates interferon production, triggers glycogen synthase to store energy fuel, enhances leukocyte function, and improves the effectiveness of vitamin C in cancer treatment. Moreover, it acts against the activation of oncogenes associated with cancer initiation and increases blood levels of lactoferrin, which inhibits bacterial growth (Cutone et al., 2020).

Despite these positive effects, it is crucial to acknowledge that uncontrolled exercises may have negative consequences for cancer patients. Studies have indicated a potential increase in thyroid cancer risk with uncontrolled and prolonged physical activities (Robsahm et al., 2010), and while some minor negativities have been noted in another study (Thomsen et al., 2023), it is essential to consider these aspects. Recognizing these potential negative effects, specialized physiotherapists and oncologists should raise awareness about the inclusion of exercise in the treatment plan. Further research is needed to clarify the effects of physical activities on cancer treatment, and personalized exercise protocols should be established. It is imperative to convey the message that exercise is a vital component of cancer treatment, akin to a powerful medicine.

### **References**

- Abdulrasool, M. D., Joda, E. O. and Alawady, A. A. (2020). The effect of psycho-physiological sports proposed in terms of the hormone endorphins serotonin and their relative results on mental fitness in the aged, *Annals of Tropical Medicine & Public Health*, 23(S13B), SP231369. doi:org/10.36295/ASRO.2020.231369
- AL-Mhanna, S. B., Ghazali, W. S. W., Mohamed, M., Rabaan, A. A., Santali, E. Y., Alestad J. H...Afolabi, H. A. (2022). Effectiveness of physical activity on immunity markers and quality of life in cancer patient: a systematic review. *PeerJ*, 10:e13664 doi:org/10.7717/peerj.13664

- Avancini, A., Sartori, G., Gkoutakos, A., Casali M., Trestini I., Tregnago D...Pilotto, S. (2020). Physical activity and exercise in lung cancer care: will promises be fulfilled? *Oncologist*, 25(3), e55e569, doi:org/10.1634/theoncologist.2019-0463
- Baran, E. (2021). Ünilateral meme kanseri tedavisi ile ilişkili üst ekstremitte lenfödeminde kompleks boşaltıcı fizyoterapinin duyuşal parametreler üzerine etkisinin incelenmesi. Hacettepe Üniversitesi Sağlık Bilimleri Enstitüsü Fizik Tedavi ve Rehabilitasyon Programı Doktora Tezi.
- Basha, M. A., Aboelnour, N. H., Alsharidah, A. S. and Kamel F. H. (2022). Effect of exercise mode on physical function and quality of life in breast cancer-related lymphedema: a randomized trial. *Supportive Care in Cancer*, 30(3), 2101-2110. Doi:org/10.1007/s00520-021-06559-1
- Bessa, A., Bosco, C., Mehrotra, S., Rowland, M., Zhang, H., Russell...Hemelrijck, M. V. (2021). Is there a role for physical activity interventions in the treatment pathway of bladder cancer? A scoping review of the literature. *BMJ Open Sport & Exercise Medicine*, 7:e000951, doi:org/10.1136/bmjsem-2020-000951
- Boice, A. and Bouchier-Hayesa, L. (2020). Targeting apoptotic caspases in cancer. *BBA - Molecular Cell Research* 1867, 118688, doi:org/10.1016/j.bbamcr.2020.118688
- Bozkurt, F. (2021) Kadın futbolcularda ppar-alpha geni polimorfizinin incelenmesi. Ondokuz Mayıs Üniversitesi Lisansüstü Eğitim Enstitüsü Beden Eğitim ve Spor Anabilim Dalı Yüksek Lisans Tezi, Proje kodu: PYO.YDS.1904.19.001.
- Brown, J. C., Ma, C., Shi, Q., Niedzwiecki, D., Zemla, T., Couture, F...Meyerhardt, J. A. (2023). Association between physical activity and the time course of cancer recurrence in stage III colon cancer. *British Journal of Sports Medicine*, 1-8, doi:org/10.1136/bjsports-2022-106445
- Capozzi, L. C., Daun, J. T., Ester, M., Mosca, S., Langelier, D., Francis, G. J...Culos-Reed, S. N. (2021). Physical activity for individuals living with advanced cancer: evidence and recommendations. *Seminars in Oncology Nursing*, 37(4), 151170 doi:org/10.1016/j.soncn.2021.151170
- Chang, J. S., Kim, T. H. and Kong, I. D. (2020). Exercise intervention lowers aberrant serum WISP-1 levels with insulin resistance in breast cancer survivors: A randomized controlled trial. *Scientific Reports*, 10, 10898, doi:org/10.1038/s41598-020-67794-w
- Chen, F. T., Hopman, R. J., Huang, C. J., Chu, C. H., Hillman, C. H., Hung, T. M. and Chang Y. K. (2020). The effect of exercise training on brain structure and function in older adults: A systematic review based on evidence from randomized control trials. *Journal of Clinical. Medicine*, 9 (4), 914 doi:org/10.3390/jcm9040914
- Chen, J., Zhou, R., Feng, Y. and Cheng, L. (2022). Molecular mechanisms of exercise contributing to tissue regeneration. *Signal Transduction Targeted Therapy*, 7, 383 doi:org/10.1038/s41392-022-01233-2
- Cormie, P., Zopf, E. M., Zhang, X., Kathryn, H. and Schmitz, K. H. (2017). The impact of exercise on cancer mortality, recurrence, and treatment-related adverse effects. *Epidemiology Reviews*, 39, 71-92, doi:org/10.1093/epirev/mxx007
- Cutone, A., Rosa, L., Ianiro, G., Lepanto, M. S., di Patti, M. C. B., Valenti, P. and Musci, G. (2020). Lactoferrin's anti-cancer properties: Safety, selectivity, and wide range of action. *Biomolecules*, 10, 456, doi:org/10.3390/biom10030456
- Da Silveira, M. P., Fagundes, K. K. S., Bizuti, M. R., Starck, É., Rossi, R. C. and e Silva D. T. R. (2021). Physical exercise as a tool to help the immune system against COVID-19: An integrative review of the current literature *Clinical and Experimental Medicine*, 21, 15-28
- Davis, A. R., Goodenough, C. G., Westerlind, K. C., Strange, R., Deaver, J. W., Ryan...Fluckey, J. D. (2022). Myokines derived from contracting skeletal muscle suppress anabolism in MCF7 breast cancer cells by inhibiting mTOR. *Frontiers Physiology*. 13,1033585, doi:org/10.3389/fphys.2022.1033585

- De Nys, L., Anderson, K., Ofosu, E. F., Ryde, G. C., Connelly, J. and Whittaker, A. C., (2022). The effects of physical activity on cortisol and sleep: A systematic review and meta-analysis *Psychoneuroendocrinology*, 143, 105843, doi:org/10.1016/j.psyneuen.2022.105843
- De Roon, M., May, A. M., McTiernan, A., Scholten, R. J. P. M., Peeters, P. H. M., Friedenreich, C. M. and Monninkhof, E. M. (2018). Effect of exercise and/or reduced calorie dietary interventions on breast cancer-related endogenous sex hormones in healthy postmenopausal women. *Breast Cancer Research*, 20, 81, doi:org/10.1186/s13058-018-1009-8
- Deb, A. A., Okechukwu, C. E., Emara, S. and Abbas, S. A. (2019). Physical activity and prostate cancer: A systematic review. *Urology & Nephrology Open Access Journal*, 7(5), 117-129.
- Dethlefsen, C., Hansen, L. S., Lillelund, C., Andersen, C., Gehl, J., Christensen J. F...Hojman, P. (2017). Exercise-Induced catecholamines activate the hippo tumor suppressor pathway to reduce risks of breast cancer development. *Cancer Research*, 77, 4894–4904, doi:org/10.1158/0008-5472.CAN-16-3125
- Docherty, S., Harley, R., McAuley, J. J., Crowe, L. A. N., Pedret, C., Kirwan, P. D...Millar, N. L. (2022). The effect of exercise on cytokines: implications for musculoskeletal health: a narrative review. *BMC Sports Science, Medicine and Rehabilitation*, 14(5).
- Emery, A., Moore, S., James, E. Turner, J. E. and Campbell, J. P. (2022). Reframing how physical activity reduces the incidence of clinically-diagnosed cancers: appraising exercise-induced immuno-modulation as an integral mechanism. *Frontiers in Oncology*, 12, 788113, doi:org/10.3389/fonc.2022.788113
- Esmailiyan, M., Nobari, H., Kargarfard, M., Amerizadeh, A., Esfarjani, F., Vaseghi...Ardigo, L. P. (2022). Effect of 12-week aerobic exercise training on chemokine ligands and their relative receptors in balb/c mice with breast cancer. *International Journal of Sport Studies for Health*, 5(2), e134187, doi:org/10.5812/intjssh-134187.
- Faris, W. I. A., Ashem, H. N., El-Ghany, M., S., El-D. and Othman E. M. (2022). Leptin and ghrelin response to aerobic exercises in post-colectomy patients. *International Journal of Recent Advances in Multidisciplinary Research*, 09(08), 7911-7916, www.ijramr.com
- Goldschmidt, S., Schmidt, M. E. and Steindorf K. (2023). Long-term effects of exercise interventions on physical activity in breast cancer patients: a systematic review and meta-analysis of randomized controlled trials. *Supportive Care in Cancer* 31, 130, doi:org/10.1007/s00520-022-07485-6
- Hayes, S. C., Steele, M. L., Spence, R. R., Gordon, L., Battistutta, D., Bashford...Eakin, E. (2018). Exercise following breast cancer: Exploratory survival analyses of two randomised, controlled trials. *Breast Cancer Research Treatment*, 167, 505–514, doi:org/10.1007/s10549-017-4541-9
- Haupt, S., Niedrist, T., Sourij, H., Schwarzinger, S. and Moser, O. (2022). The impact of exercise on telomere length, dna methylation and metabolic footprints. *Cells*, 11, 153, doi:org/10.3390/cells11010153
- Hauth, F., De-Colle, C., Weidner, N., Heinrich, V., Zips D. and Gani, C. (2021). Quality of life and fatigue before and after radiotherapy in breast cancer patients. *Strahlenther Onkology*, 197(4), 281-7, doi:org/ 10.1007/s00066-020-01700-1
- Hilfiker, R., Meichtry, A., Eicher, M., Balfe, L. N., Knols, R. H., Verra, M. L. and Taeymans, J. (2018). Exercise and other non-pharmaceutical interventions for cancer-related fatigue in patients during or after cancer treatment: A systematic review incorporating an indirect comparisons meta-analysis. *British journal of sports medicine*, 52(10), 651–658, doi:10.1136/bjsports-2016-096422
- Huneidi, S. A., Wright, N. C., Atkinson, A., Bhatia, S. and Singh, P. (2018). Factors associated with physical inactivity in adult breast cancer survivors-A population-based study. *Cancer Medicine*, 7(12), 6331-6339, doi:10.1002/cam4.1847
- Iwase, T., Wang, X., Shrimanker, T. V., Kolonin, M. G. and Ueno, N. T. (2021). Body composition and breast cancer risk and treatment: Mechanisms and impact. *Breast Cancer Research Treatment*, 186, 273-283, doi:org/10.1007/s10549-020-06092-5

- Kim, J., Lee, J., Oh, J. H., Chang, H. J., Sohn, D. K., Shin, A. and Kim, J. (2020). Plasma inflammatory biomarkers and modifiable lifestyle factors associated with colorectal cancer risk. *Clinical Nutrition*, 39(9), 2778–2785, doi:org/10.1016/j.clnu.2019.12.005
- Lee, J. H. and Jun, H. S. (2019). Role of myokines in regulating skeletal muscle mass and function. *Frontiers Physiology*, 10(42) 1-9, doi:org/10.3389/fphys.2019.00042
- Lee, M. K. and Oh, J. (2021). Patient-reported outcomes of regular aerobic exercise in gastric cancer. *Cancers*, 13, 2080. doi:org/10.3390/cancers13092080.
- Lee, S. and Margolin, K. (2011). Cytokines in cancer immunotherapy, *Cancers (Basel)*, 3(4), 3856–3893. Doi:org/10.3390/cancers3043856
- Ligibel, J. A., Bohlke, K., May, A., M., Clinton, S. K., Demark-Wahnefried, W., Gilchrist, S...Alfano, C. M. (2022). Exercise, diet, and weight management during cancer treatment: ASCO Guideline *Journal of Clinical Oncology*, 40(22), 2491-2507, Doi:org/10.1200/JCO.22.00687
- Marques, A., Marconcin, P., Werneck, A. O., Ferrari, G., Gouveia, E. R., Kliegel, M... Ihle, A. (2021). Bidirectional association between physical activity and dopamine across adulthood—A Systematic Review. *eBrain Science*, 11(7), 829, doi:org/10.3390/brainsci11070829
- Metcalfe, R. S., Kemp, R., Heffernan, S. M., Churm, R., Chen, Y. C., Ruffino, J. S...Orange, S. T. (2021). Anticarcinogenic effects of exercise-conditioned human serum: evidence, relevance and opportunities. *European Journal of Applied Physiology*, 121, 2107-2124, doi:org/10.1007/s00421-021-04680-x
- Misiag, W., Piszczyk, A., Szymanska-Chabowska, A. and Chabowski, M. (2022). Physical Activity and Cancer care-a review. *Cancers*, 14, 4154, doi:org/10.3390/cancers14174154
- Moon, H.S. and Mantzoros, C. S. (2014). Regulation of cell proliferation and malignant potential by irisin in endometrial, colon, thyroid and esophageal cancer cell lines. *Metabolism*, 63(2), 188-193, doi:org/10.1016/j.metabol.2013.10.005.
- Morishita, S., Hamaue, Y., Fukushima, T., Tanaka, T., Fu J. B. and Nakano, J. (2020). Effect of exercise on mortality and recurrence in patients with cancer: A Systematic Review and Meta-Analysis *Integrative Cancer Therapies*, 19, 1-10, doi:org/10.1177/1534735420917462
- Nazik, E., Öztunç, G. and Şahin, B. (2014). Effects of progressive relaxation training on sleep quality and pain in patients with breast cancer undergoing chemotherapy. *Anatolian Journal of Nursing and Health Sciences*, 17(3), 171-178
- Nuri, R., Moghaddasi, M. and Izadpanah, A. (2016). Effect of aerobic exercise on leptin and ghrelin in patients with colorectal cancer. *Journal of Cancer Research and Therapeutics*, 12(1), 169-174, doi:org/10.4103/0973-1482.155982
- Onerup, A. (2021). The role of physical activity for recovery after surgical procedures. Department of Surgery Institute of Clinical Sciences Sahlgrenska Academy, University of Gothenburg, ISBN 978-91-8009-159-6 (PDF), <http://hdl.handle.net/2077/67125>
- Oruç, Z. and Kaplan, M. A., (2019). Effect of exercise on colorectal cancer prevention and treatment, *World Journal Gastrointest Oncology*, 11(5), 348-366, doi:org/10.4251/wjgo.v11.i5.348
- Pahlavani, H. A. and Veisi, A. (2018). The effect of aerobic and anaerobic training with melatonin consumption on the expression of apoptotic genes BAX and BCL2 myocardial in rats after ischemic reperfusion. *Journal of Human Sport and Exercise*, 13(2), 454–66, doi:org/10.14198/jhse.2018.13.Proc2.29.
- Perego, S., Sansoni, V., Ziemann, E. and Lombardi, G. (2021). Another weapon against cancer and metastasis: physical-activity-dependent effects on adiposity and adipokines. *International Journal of Molecular Sciences*, 22, 2005. doi:org/10.3390/ijms22042005
- Permadi, A. (2019). The benefits of aerobic training for improving quality of life: A Critical Review of Study, *WMJ*, 4(2), 57-60, doi:org/10.22225/wmj.4.2.1016.57-60

- Piroux, E., Caty, G., Nana, F. A. and Reychler, G. (2020). Effects of exercise therapy in cancer patients undergoing radiotherapy treatment: A narrative review, 8, doi:org/10.1177/2050312120922657
- Pollán, M., Casla-Barrio, S., Alfaro, J., Esteban, C., Segui-Palmer, M.A., Lucia, A. and Martín, M. (2020). Exercise and cancer: a position statement from the Spanish Society of Medical Oncology. *Clinical and Translational Oncology*, 22, 1710-1729, doi:org/10.1007/s12094-020-02312-y
- Rasmussen, G. H. F., Kristiansen, M., Arroyo-Morales, M., Voigt, M. and Madeleine, P. (2020). Absolute and relative reliability of pain sensitivity and functional outcomes of the affected shoulder among women with pain after breast cancer treatment. *Plos one*, 15(6), e0234118 doi:10.1371/journal.pone.0234118
- Robsahm, T. E., Hestvik, U. E., Veierod, M. B., Fagerlie, A., Nystad, V., Engebretsen, L. and Tretli, S. (2010). Cancer risk in Norwegian world class athletes, *Cancer Causes & Control*, 21(10), 1711-1719, doi:org/10.1007/s10552-010-9600-z
- Roscoe, C. M. P., Pringle, A., Chandler, C., Faghy, M. A. and Barratt, B. (2022). The role of physical activity in cancer recovery: an exercise practitioner's perspective. *International Journal of Environmental Research Public Health*, 19, 3600, doi:org/10.3390/ijerph19063600
- Schink, K., Herrmann, H. J., Schwappacher, R., Meyer, J., Orlemann, T., Waldmann, E... Zopf, Y. (2018). Effects of whole-body electromyostimulation combined with individualized nutritional support on body composition in patients with advanced cancer: a controlled pilot trial. *BMC Cancer*, 18, 886 doi:org/10.1186/s12885-018-4790-y
- Schwappacher, R., Dieterich, W., Reljic, D., Pilarsky, C., Mukhopadhyay, D., Chang, D. K...Zopf, Y. (2021). Muscle-Derived Cytokines Reduce Growth, Viability and Migratory Activity of Pancreatic Cancer Cells *Cancers (Basel)*, 29;13(15), 3820, doi:org/10.3390/cancers13153820
- Severinsen, M. C. K. and Pedersen, B. K. (2020). Muscle-Organ crosstalk: The emerging roles of myokines. *Bioggy Medicine, Endocrine Reviews*. 41(4), 594-609, doi:org/10.1210/endrev/bnaa016
- Shao, W., Zhang, H., Qi H. and Zhang, Y. (2022). The effects of exercise on body composition of prostate cancer patients receiving androgen deprivation therapy: An update systematic review and meta-analysis. *PLoS One*, 17(2), doi:org/10.1371/journal.pone.0263918
- Sundari, L. P. R. and Arsani, N. L. K. A. (2022). Regular physical exercise increase of growth hormone (gh) and insulin-like growth factor-1 (igf-1) activity in elderly improve the aging process and quality of life: A mini review. *Biomedical & Pharmacology Journal*, 15(2), 883-890, doi:org/10.13005/bpj/2422
- Swain, C. T. V., Ann, E., Drummond, A. E., Boing, L., Milne, R. L., Dallas, R...Lynch, B. M. (2022). Linking physical activity to breast cancer via sex hormones, part 1: the effect of physical activity on sex steroid hormones. *Cancer Epidemiol Biomarkers Prevention*, 31(1), 16-27, doi:org/10.1158/1055-9965.EPI-21-0437.
- Teixeira, G. R., Mendes, L. O., Veras, A. S. C., Thorpe, H. H. A., Fávaro, W. J., Chuffa, L. G. A... Martinez F.E. (2020). Physical resistance training-induced changes in lipids metabolism pathways and apoptosis in prostate. *Lipids in Health and Disease*, 19, 14, doi:org/10.1186/s12944-020-1195-0
- Thomsen, S. N., Lahart, I. M., Thomsen, L. M., Fridh, M. K., Larsen, A., Mau-Sørensen, M... Simonsen C., (2023). Harms of exercise training in patients with cancer undergoing systemic treatment: a systematic review and meta-analysis of published and unpublished controlled trials. *EclinicalMedicine*, 6(59), 101937. doi:org/10.1016/j.eclinm.2023.101937.
- Torregrosa, C., Chorin, F., Beltran, E. E. M., Neuzillet, C. and Cardot-Ruffino, V. (2022). Physical activity as the best supportive care in cancer: The clinician's and the researcher's perspectives. *Cancers*, 14(21), 5402. doi:org/10.3390/cancers14215402.
- Wiestad, T. H., Raastad, T., Nordin, K., Igelström, H., Henriksson, A., Demmelmaier, I. and Berntsen, S. (2020). The Phys-Can observational study: adjuvant chemotherapy is associated with a reduction whereas physical activity level before start of treatment is associated with maintenance of maximal oxygen uptake in patients with cancer. *BMC Sports Science*, 12(53), doi:org/10.1186/s13102-020-00205-9

- Wang, Q. and Zhou W. (2021). Roles and molecular mechanisms of physical exercise in cancer prevention and treatment. *Journal of Sport and Health Science*, 10(2), 201-210, doi:org/10.1016/j.jshs.2020.07.008.
- Yang, H., Yang, Z., Pan, H. and Zhou, Q. (2021). Effects of physical activity on sleep problems in breast cancer survivors: a meta-analysis. *Supportive Care in Cancer*, 29(24), 1-10, doi:org/10.1007/s00520-020-05914-y
- Yang, Y-P., Pan, S-J., Qui, S-L. and Tung, T-H. (2022). Effects of physical exercise on the quality-of-life of patients with haematological malignancies and thrombocytopenia: A systematic review and meta-analysis. *World Journal of Clinical Cases*, 10(10), doi:org/10.12998/wjcc.v10.i10.3143.
- Yousaf, R. and Marwat, M. K. (2022). Effect of moderate level aerobic training on maximum oxygen consumption and cardiovascular fitness of non-athlete students GESR VII, (1) 15, doi:org/10.31703/gesr.2022(VII-I).15
- Zerhouni, M. and Piskounova, E. (2022). Running to outcompete metastasis. *Cancer Research*, 82 (22), 4124– 4125, doi:org/10.1158/0008-5472.CAN-22-2898
- Zhao, H., Cheng, R., Song, G., Teng, J., Shen, S., Fu, X...Liu C. (2022). The effect of resistance training on the rehabilitation of elderly patients with sarcopenia: A Meta-Analysis. *International Journal of Environmental Research and Public Health*, 19, 15491, doi:org/10.3390/ijerph192315491
- Zheng, A. S., Zhang, L., Yang, J., Xiaomeng, Yin, X., Zhang, T... Ma, X. (2022). Physical activity prevents tumor metastasis through modulation of immune function. *Frontiers in Pharmacology*. 13, 1034129. doi:org/10.3389/fphar.2022.1034129
- Zhou, Y., Jia, N., Ding, M. and Yuan K. (2022). Effects of exercise on inflammatory factors and IGF system in breast cancer survivors: a meta-analysis. *BMC Women's Health*, 22, 507, doi:org/10.1186/s12905-022-02058-5
- Zhu, C., Ma, H., He, A., Li, Y., He, C. and Xia, Y. (2022). Exercise in cancer prevention and anticancer therapy: Efficacy, molecular mechanisms and clinical information. *Cancer Letters*, 544, 215814 doi:org/10.1016/j.canlet.2022.215814