THE EUROPEAN SOCIETY OF MEDICINE
Medical Research Archives, Volume 14 Issue 5

REVIEW ARTICLE

Is There a Relationship Between Chronic Stress and Cancer Development? - A Review:

Alexandra Paul [1] and Tamara Kalir, M.D., PhD.[2]

[1] Barnard College of Columbia University
[2] The Icahn School of Medicine at Mount Sinai

OPEN ACCESS

PUBLISHED
31 May 2026

CITATION
Paul, A., and Kalir, T., 2026. Is There a Relationship Between Chronic Stress and Cancer Development? - A Review. Medical Research Archives, [online] 14(5).

ISSN
2375-1924

ABSTRACT

Chronic stress has been increasingly investigated as a factor influencing cancer development and progression. This review examines the biological and psychosocial mechanisms linking chronic stress to oncogenesis, including prolonged activation of the hypothalamic-pituitary-adrenal (HPA) axis, inflammation, immune dysregulation, and β-adrenergic signaling. Evidence from mechanistic studies demonstrates that chronic stress promotes tumor-supportive environments by impairing immune surveillance, increasing inflammatory cytokine production, and altering cellular signaling pathways. Epidemiologic findings remain heterogeneous, with some studies showing modest associations between stress and cancer incidence, while others report no consistent relationship. Additionally, metabolic comorbidities and psychosocial factors, such as social support, can further influence these effects. Overall, while causality is not definitively established, chronic stress appears to contribute to biological conditions that may facilitate cancer development and progression. Future research integrating objective stress biomarkers and longitudinal designs is needed to clarify these relationships.

Introduction

Acute stress plays an important role in daily life by creating motivation to complete tasks, increasing alertness, and fostering adaptability. However, when stress becomes chronic, lasting for long periods of time without resolution, it transitions from being helpful to harmful.

Chronic stress is defined in this review as an extended activation of the hypothalamic-pituitary-adrenal (HPA) axis, and as a result, a mental and physical strain and state of alertness that can persist for weeks, months, or even years[1],[11]. Chronic stress can be recognized by an increase in cortisol levels and inflammatory markers that can be disruptive[7],[10]. It can be objectively measured through the presence of C-reactive proteins and cardiovascular variability. The strain can become mentally and physically burdensome, with impacts reaching hormonal balances, the immune system, and sleep quality[11],[16]. Individuals facing economic burdens, chronic health conditions, and systemic healthcare barriers are disproportionately impacted by chronic stress. Increasingly, researchers are investigating whether chronic stress can also affect cancer development[11],[19].

This review studies existing literature on the relationship between chronic stress and cancer development, and whether chronic stress may not only correlate with elevated cancer risk, but also aggravate physiological pathways already involved in tumor growth and advancement[11],[12],[19].

Methods

A narrative literature review was conducted using the PubMed database to identify studies examining the relationship between chronic stress and cancer development. The search covered publications from 2000 to 2025 and used combinations of the keywords "cancer," "chronic stress," "immune dysfunction," "inflammation," and "β-adrenergic signaling."

Articles were included if they (1) examined chronic psychological or physiological stress, (2) investigated mechanistic links between stress and cancer biology, and (3) focused on adult human populations or relevant animal models. Both primary research studies and review articles were considered. Studies were excluded if they focused on pediatric populations or lacked relevance to cancer-related outcomes.

A total of 22 articles were selected based on relevance to the mechanistic and clinical relationship between chronic stress and cancer. Emphasis was placed on studies addressing inflammation, immune dysregulation, neuroendocrine signaling, and epidemiologic associations.

Results

MECHANISTIC FOUNDATIONS:

In Murata[1], inflammation is centered as a critical link between cancer and stress. Chronic stress has been shown to prolong low-grade inflammation, and inflammation is an established trademark of cancer. Murata[1] reported that infection and inflammation are responsible for approximately 25% of cancer-causing factors. Murata[1] further explained that inflammation-related cancers are denoted by mutagenic DNA lesions, like 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-oxodG) and 8-nitroguanine. Chronic inflammation causes different types of damage to lipids, nucleic acids, and proteins through reactive oxygen/nitrogen (ROS/RNS) generation, leading to tissue damage. The harmed tissue can then activate stem cells for tissue regeneration. Stem cells are injured by ROS/RNS from inflammation, and the mutations can compound, which could then lead to the creation of cancer cells. Several studies have suggested that inflammation-associated DNA damage leads to cancer development with aggressive clinical elements.

In a primary study conducted by Murata[1], a hydrogen-peroxide-resistant cholangiocyte model was exposed to prolonged low-dose oxidative stress, which demonstrated a marked accumulation of 8-oxodG, as well as increased cell growth and expression of antioxidant enzymes. These chronically stressed cells showed large downregulation of the tumor-suppressor gene EBF1, and experimental EBF1 knockdown in normal cholangiocytes increased stemness markers (CD133 and Oct3/4) and enhanced migratory capacity. In patient samples, low EBF1 expression with high 8-oxodG formation was linked with significantly poorer survival. Overall, these findings suggest that prolonged oxidative stress during chronic inflammation promotes DNA damage and tumor suppressor dysfunction, creating conditions that support cholangiocarcinoma initiation and proliferation. Chronic stress-mediated inflammation may therefore create conditions conducive to oncogenesis.

Petrinovic et al[2] reported that chronic psychological stress has been pinpointed as a factor contributing to the growth and development of cancer. They cite Feng et al[3], who demonstrated that chronically elevated glucocorticoids during long-term restraint stress suppress tumor protein p53 expression and diminish its tumor-suppressive function, directly contributing to stress-enhanced tumorigenesis following irradiation. Long-term exposure to chronic stress disturbs the homeostatic communication between the endocrine and immune systems, thereby moving the immune system to a proinflammatory state. Zong et al[4] showed that chronic stress-activated β-adrenergic signaling induces p53 protein degradation in gastric epithelial cells, leading to malignancies under continuous catecholamine exposure. Chronic low-level inflammation driven by stress, along with reduced and weakened immune defenses, plays a role in the initiation and advancement of cancer. In addition to weakening immune surveillance, catecholamines, hormones that are involved in stress responses themselves, directly promote tumor growth. Lin et al[5] found that epinephrine and norepinephrine stimulate proliferation of colorectal carcinoma cells through ERK1/2 activation in nude mice, while Koh et al[6] established that β-adrenergic blockade with propranolol inhibits ERK signaling, induces G1/S arrest, and prompts apoptosis in gastric cancer cells. Beyond establishing a tumor-promoting inflammatory environment, cytokines created by tumors can circulate through the body and

interfere with stress regulation. Clinical evidence reinforces this dysregulation. Cancer patients frequently exhibit altered HPA axis activity and abnormal cortisol secretion patterns[7]. High tumor grade and advanced stage disease are linked with heightened cortisol levels[8,9]. Additionally, HPA axis impairment under chronic stress contributes to immunosuppression[10] and escalates risk for anxiety and depression in cancer patients[7], adding further psychological and biological strain.

Dai et al[11] explored how protracted sympathetic nervous system (SNS) and HPA axis activation contribute to oncogenic biology. They demonstrated that chronic stress can prompt tumorigenesis and lead to cancer development. Feng et al[3] demonstrated in a murine chronic-restraint stress model that elevated glucocorticoids suppress p53 regulation by inducing serum/glucocorticoid-regulated kinase 1 (SGK1), which in turn activates mouse double minute 2 homolog (MDM2) and accelerates p53 deterioration, compromising DNA repair and apoptosis, substantially elevating cancer susceptibility. Under conditions of chronic stress, the long-term activation of the HPA axis and the SNS leads to impaired functioning of the hippocampus and prefrontal cortex. These dysregulated stress pathways release high levels of glucocorticoids that impair brain feedback loops and correlate with poorer clinical outcomes. For example, breast cancer patients with elevated glucocorticoids during disease progression show lower survival and greater metastatic signaling caused by receptor tyrosine kinase-like orphan receptor 1 (ROR1), which is linked with cancer metastasis[11]. The hormones released as a result of the stimulation of these systems, in turn, propel tumor emergence and cancer progression through multiple mechanisms. Catecholamines released during chronic stress can activate β-adrenergic receptors on tumor cells, activating the cyclic adenosine monophosphate-protein kinase A (cAMP-PKA) pathway that enhances angiogenesis and motivates tumor invasion. These adrenergic pathways also alter cellular metabolism and cause p53 degradation, thus lending to more aggressive tumor behavior, specifically across breast, prostate, and pancreatic cancer models. Dai et al[11] suggested that stress management is necessary for individuals diagnosed with cancer and healthy people alike. This is supported by evidence that blocking β-adrenergic signaling or lowering stress-related hormone output can stop cell-cycle advancement, cause apoptosis, lessen metastasis, and improve anti-tumor immune responses.

CHRONIC STRESS AND IMMUNE DYSREGULATION:

Along with prolonging inflammation, chronic stress weakens the body's immune system and thereby its ability to identify and destroy cancerous cells. Physiologically, the weakening of the immune system under chronic stress is brought about by continuous neuroendocrine signaling. Sustained activation of the HPA axis leads to increased cortisol levels, which, over time, suppress lymphocyte proliferation and decrease antigen presentation. Moreover, a manifestation of immune dysregulation is the blocking of the cytotoxic activity of natural killer (NK) cells. NK cells are essential in identifying tumor antigens and triggering apoptosis in abnormal cells; therefore, their suppression fundamentally undermines early anti-tumor defense. Overall, through detecting tumor antigens, the immune system acts as a frontline defense against the proliferation of malignant cells. Chronic stress can diminish the capabilities of both the adaptive and innate immune responses.

Zhang et al[12] affirm that chronic stress strengthens the tumor-induced immune suppressive cells and hinders the cytotoxicity of cellular immunity, thereby facilitating hematogenous and lymphatic metastasis. They further described that chronic stress suppresses type I cytokine secretion, elevates tumor-infiltrating CD25 regulatory T cells, and decreases CD4 T-cell infiltration. These changes are coupled with a shorter time to ultraviolet-B-triggered squamous cell carcinoma appearance and increased tumorigenesis after carcinogen exposure in animal models. Zhang et al[12] showed that lymphoid cells taken from chronically stressed mice have faster tumor growth when moved to irradiated hosts, indicating that changes due to stress in immune cells are directly connected to tumor progression.

Zhang et al[12] further emphasize that chronic stress enhances metastatic potential by increasing tumor secretion of matrix metalloproteinase-2 (MMP2), an enzyme that promotes tumor activity, and by facilitating stress-mediated dysregulation of tumor-infiltrating lymphocytes, which supports a number of steps in the metastatic pathway. Furthermore, they establish that the success of cancer treatments is sabotaged by chronic stress, as the immune system continues to be unable to respond properly. Collectively, these changes give rise to an immunosuppressive state conducive to oncogenic metastasis.

Cole and Sood[13] demonstrate that epinephrine and norepinephrine activate β-receptors on tumor and stromal cells. β-adrenergic signaling is involved in the development and progression of cancer, inflammation, and apoptosis. It is shown that in numerous experimental cancer models, the activation of the sympathetic nervous system advanced the metastasis of solid epithelial tumors and the spreading of hematopoietic malignancies by way of beta-adrenergic receptor-mediated protein kinases. Research on how the sympathetic nervous system influences the tumor environment and cancer cell biology demonstrates a molecular basis to the long-suspected link between chronic stress and cancer progression, showing a promising new target for therapeutic intervention.

Dong et al[14] reported that sympathetic nerve fibers innervate many solid tumors and exert a significant influence on cancer behavior. They similarly reported that adrenergic signaling is a significant contributor to the regulation of tumor activity at both the cellular and microenvironmental levels. Dong et al[14] noted that most components of the tumor microenvironment, including epithelial, stromal, vascular, and immune cells, possess adrenergic receptors, allowing norepinephrine and epinephrine to impact multiple cancer-related processes. Tumor-suppressing effects are mediated by various types of adrenergic receptors. These mixed effects arise because different adrenergic receptor types regulate various biological pathways, with some amplifying tumor

growth while others counteract it. Thus, the use of specific antagonists may inhibit adrenergic-regulated functions. Dong et al.[14] highlight that many adrenergic receptors are G-protein-coupled receptors with well-established antagonists already in clinical use, making them favorable candidates for drug repurposing. Exploring established adrenoreceptor antagonists through drug repurposing may help mitigate this issue in the future.

CHRONIC STRESS, CANCER, AND METABOLIC COMORBIDITIES

Metabolic comorbidities continue to amplify the mechanisms of cancer and chronic stress. Research indicates that diabetes itself is linked with higher rates of cancer, with large pooled analyses showing significant increases in both cancer incidence and cancer-related deaths among individuals with metabolic disease. Avogaro[15] reported that stress, diabetes, and obesity all intersect through converging pathways of systemic immune deterioration and inflammation. Avogaro[15] further noted that prolonged stress can intensify these metabolic issues by creating hormonal patterns that push the body toward greater inflammation and layered energy use, emphasizing the same biological pressures seen in diabetes and obesity. Increased adiposity and hyperglycemia elevate circulating pro-inflammatory cytokines and simultaneously decrease the efficiency of cells. These metabolic perturbations are not insignificant. Continuous elevations in glucose and increased adipose tissue are linked with strengthened inflammatory signaling and greater oxidative stress, creating an environment that can promote malignancies. Avogaro[15] also reported that the American Cancer Society and the American Diabetes Association have issued a shared statement stating that type two diabetes is correlated with an elevated risk for pancreatic, liver, breast, colon, and rectum cancers. Avogaro[15] further explained that these patterns remain true across diverse populations, with meta-analyses showing more than a 20% increase in overall cancer risk among people with type 2 diabetes, and cohort studies demonstrating similarly elevated risk in type 2 diabetes and even prediabetes. Finally, Avogaro[15] suggested that the combination of metabolic disease with ongoing stress can potentially heighten vulnerability even further, suggesting an added effect in individuals who experience both mental and physiological strain.

PSYCHOSOCIAL DIMENSIONS OF CANCER AND CHRONIC STRESS

Antoni et al[16] reported that psychosocial stress in individuals with cancer corresponded with measurable suppression of immune response. They established that protective immunity is especially important for eliminating immunogenic cancers, for example, basal cell carcinoma and squamous cell carcinoma (SCC), tumors that are made immunogenic as a result of immunotherapy, and human papillomavirus (HPV) related anal, oral, and cervical cancers. Work in this area also emphasizes that persistent psychological strain can interfere with how immune cells are able to reach tissues, changing the balance of responses required for effector tumor surveillance. Antoni et al[15] further noted that several pathways and mechanisms have been identified by which chronic stress negatively impacts protective immunity. Glucocorticoid and catecholamine hormones are two significant physiologic mediators of suppression of protective immunity through chronic stress. These hormonal shifts influence multiple areas of immune coordination, including T-cell proliferation and responsiveness to developing tumors. Furthermore, in animal and human studies, it has been shown that chronic stress leads to suppression of cell-mediated immunity, graft rejection, and macrophage-led antimycobacterial activity. Studies also show that prolonged stress can decrease the presence of the immune population within tumors, with decreases in CD4 and CD8 T-cell activity. In animal models, higher trait anxiety measured before tumor induction predicted elevated tumor burden when exposed to chronic stress. This is consistent with animal studies that demonstrate that mice that have stronger baseline anxiety traits show more immunosuppression and increased vulnerability to tumor growth under stress. Studies in patients with different types of later-stage cancers have shown that chronic stress can suppress necessary immune responses against cancer through glucocorticoid and catecholamine-moderated pathways. Antoni et al[15] found that depression was also connected to suppressed T-cell cytokine production and NK cell cytotoxicity around the tumor microenvironment in patients diagnosed with ovarian cancer. Additionally, psychological adversity such as depression can increase inflammatory signaling within tumors, and even correlate with shorter overall survival in some cancers. Conversely, individuals in the same situation who had social support, which is often seen as a shield against chronic stress, were associated with higher NK cell cytotoxicity. Finally, in patients with breast cancer who had less advanced disease, decreased anxiety in the weeks following their surgeries was correlated with increased production of IL-2 after anti-CD3 stimulation. In contrast, another study found that individuals with less advanced breast cancer but higher levels of stress had lower NK cell cytotoxicity and lower T-cell proliferation. Studies also demonstrated, however, that stress-management interventions could relatively restore immune abilities, suggesting that the pathway is capable of change. This provides hope that while chronic stress creates complications for cancer patients, improvement and recovery of these processes is possible.

Pinquart et al[17] conducted a meta-analysis examining the relationships between subject-discerned social support, marital status, and size of network with cancer survival. They reported that biological mediation is one potential explanation, including neuroendocrine pathways connected to stress. They give the example that social support might hinder the impact of endocrine changes that are directly correlated with stress, which are ultimately associated with tumor progression. Turner-Cobb et al[18] discovered an association between increased levels of social support and decreased cortisol levels in metastatic breast cancer patients. Pinquart et al[17] further explained that the size of an individual's social network could influence their health behavior. They again give an example, saying that if an individual is connected to a larger social network (through friends, family, or marriage), those people may encourage that

individual to seek healthcare earlier on, leading to an earlier diagnosis and treatment. Finally, they write that the relationship between improved cancer prognosis and social network might be psychologically regulated. They cite that lower levels of social support can be related to depression, which could negatively impact response to treatment and willingness to participate in treatment. Pinquart et al[17] established evidence for the association of social networks with longevity in individuals with cancer. Controlled studies showed a 12-25% reduction in relative mortality risk among patients with strong perceived social support, marital status, and extensive social networks.

EPIDEMIOLOGIC EVIDENCE

While mechanistic data provide biological plausibility for a link between chronic stress and oncogenesis, the human epidemiologic evidence concerning the development of cancer remains heterogeneous. Several large-scale reviews and cohort studies demonstrate this variability.

Cooper et al[19] found that psychological stress, depression, or anxiety are associated with a small but measurable increase in cancer incidence, with effect size varying by cancer and stressor type. Specifically, meta-analyses showed that exposure to stressful life events is associated with an increased risk of breast cancer, including a pooled relative risk of 1.11 (95% CI 1.03-1.19) across 11 cohort studies, and an odds ratio of 1.51 (95% CI 1.15-1.97) when both cohort and case-control studies were included. More severe life events were associated with an even greater elevation in risk (OR 2.07; 95% CI 1.06-4.03).

However, Cooper et al[19] also emphasized substantial heterogeneity across studies, as a large systematic review summarizing 44 cohort and case-control studies reported positive associations in 26 studies, while 18 studies showed no association, emphasizing the variability in stress measurement and population characteristics. In contrast to life-event stress, occupational stress, and work-strain measures showed little to no consistent association with cancer incidence, indicating that the intensity, length, and personal experience of stress exposure may be important variables in physiological impact.

Pham et al[20] conducted a Dutch population-based cohort study that used hair cortisol and hair cortisone as biomarkers of chronic biological stress in 6,341 cancer-free participants, with incident cancers identified prospectively through linkage to the Dutch Nationwide Pathology Databank. Neither hair cortisol (HR 0.993; 95% CI 0.740 - 1.333) nor hair cortisone (HR 1.113; 95% CI 0.738-1.678) was associated with cancer incidence. However, after adjustment for age and inclusion of sex as moderators, hair cortisone, which is a marker of long-term glucocorticoid exposure, was associated with subsequent cancer incidence (HR 6.403; 95% CI 1.110-36.92). No metabolic syndrome components acted as confounders, indicating that the observed association was not explained by measured metabolic factors. These results demonstrate the sensitivity of epidemiologic associations to demographic adjustment.

In contrast, Schoemaker et al[21] conducted a large prospective cohort study from the United Kingdom involving approximately 106,000 women and identified 1,783 incident breast cancer cases, and found no consistent association between overall breast cancer risk and either perceived frequency of stress or adverse life events in the five years preceding enrollment. However, subgroup analyses revealed modest associations, including an increased risk of estrogen receptor-negative breast cancer after divorce (RR 1.54; 95% CI 1.01-2.34), and an elevated breast cancer risk among women who experienced maternal death before age 20 (RR 1.31; 95% CI 1.01-1.67), though this latter association decreased after excluding mothers with breast or ovarian cancer. Overall, the authors concluded that perceived stress and recent adverse life events were not consistently associated with breast cancer risk, illustrating the variability in stress-cancer associations by population and tumor subtype.

Kennedy et al[22] conducted a nationwide cohort study in Sweden examining psychological stress resilience measured in late adolescence as a predictor of adult cancer risk, utilizing data from 284,257 men who underwent standardized stress-resilience assessment during compulsory military enlistment at a median age of 18 years old. Compared with men with high stress resilience, those with the lowest resilience exhibited substantially increased risks of liver cancer (HR 4.73; 95% CI 2.73-8.19) and lung cancer (HR 2.75; 95% CI 2.02-3.74), after adjustment for childhood socioeconomic factors. However, low resilience was also associated with decreased risks of prostate cancer and malignant melanoma. The findings suggest that stress resilience in adolescence may influence adult cancer risk plausibly through social and behavioral pathways.

Discussion

The evidence reviewed collectively supports biologically plausible pathways through which chronic stress may influence cancer development, yet the relationship is multifaceted and modulated by numerous behavioral, genetic, and environmental influences. Mechanistic studies consistently demonstrate that chronic activation of the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system (SNS) exerts significant downstream effects on immune surveillance and inflammatory regulation, processes central to oncogenesis. The convergence of neuroendocrine and immune dysregulation under sustained stress exposure provides a credible physiological context for understanding how psychosocial stressors may contribute to cancer development and advancement.

Inflammation is highlighted as a central mediator of these processes. The chronic elevation of inflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP) creates an environment that is favorable to genomic instability and angiogenesis. These biological disruptions are reflected by the subduing of natural killer (NK) cell cytotoxicity and decreased T-cell proliferation, which are key immune functions necessary for tumor surveillance. As

a result, individuals under persistent stress may experience a decline in anti-tumor immunity alongside heightened inflammatory signaling, creating a dual pathway conducive to malignant formation and progression.

The role of beta-adrenergic signaling offers additional insight into how stress hormones can shape the tumor microenvironment. The activation of beta-receptors by catecholamines such as epinephrine and norepinephrine creates a favorable environment for pro-metastatic cellular behaviors, including increased vascularization and resistance to apoptosis. The growing body of literature proposing beta-adrenergic antagonists as potential adjunctive therapies reflects both the therapeutic potential and clinical relevance of targeting stress-related pathways in oncology. Comorbid metabolic conditions such as obesity and diabetes further impact these mechanisms. Chronic stress not only contributes to these metabolic disorders through dysregulated glucose metabolism and adipose inflammation, but these same pathophysiological states reinforce oncogenic signaling through shared hormonal routes. Thus, the intersection of stress and metabolism in the context of cancer demonstrates the systemic nature of stress-related carcinogenesis.

Aside from molecular and physiological pathways, psychosocial research demonstrates the profound role of social and emotional factors in moderating cancer outcomes. The evidence indicates that social support acts as a physiological buffer by modulating cortisol release and immune function. These supports have been associated with more favorable immune profiles and, in some studies, better outcomes. Conversely, social isolation and chronic anxiety and depression seem to exacerbate immunosuppression and inflammatory dysregulation, possibly resulting in poorer clinical outcomes. These outcomes show that the impact of chronic stress extends beyond psychological discomfort, playing a role in tangible biological processes with measurable consequences for survival.

Epidemiological findings, however, remain inconsistent. While several large-scale studies and meta-analyses suggest a modest association between chronic stress and overall cancer incidence, others reveal null or reduced effects when controlling for confounding factors such as genetic variables or socioeconomic status. Such heterogeneity may come from methodological differences in stress measurement, follow-up duration, or the challenge of isolating stress as an independent variable within the network of possible carcinogenic influences. Emerging tools for quantifying chronic stress exposure can offer greater precision of measurement in future research.

This review has several limitations. As a narrative review, it is subject to selection bias and does not follow a fully systematic methodology. Additionally, variability in how chronic stress is defined and measured across studies limits direct comparison of findings. Many physiological insights are derived from animal models, which may not fully translate to human populations. Furthermore, the epidemiologic studies may have been confounded by socioeconomic or genetic factors, making it difficult to isolate stress as an independent variable. These limitations demonstrate the necessity for standardized measures and longitudinal human studies.

Overall, while causality remains difficult to establish, the general body of clinical and psychosocial evidence substantiates a meaningful connection between chronic stress and cancer-related biology. Chronic stress should therefore be regarded not merely as an emotional concern, but as a factor capable of influencing cancer susceptibility and progression, as well as response to treatment.

Conclusion

The relationship between chronic stress and cancer development is both complex and biologically credible. Chronic activation of the HPA axis and SNS generates immunologic and hormonal disturbances that can lead to oncogenesis through inflammation, immune suppression, and modified cellular signaling. While epidemiologic studies have mixed results, physical evidence converges to support the idea that chronic stress can create physiological conditions that facilitate tumor development and progression.

Recognizing how chronic stress interacts with metabolic and psychosocial factors demonstrates the need for cancer prevention and treatment strategies that include behavioral and social dimensions rather than relying only on pharmacologic approaches. Addressing stress as an alterable biological variable through stress-reduction intervention and psychosocial support may improve psyachological well-being, biological resilience, and treatment outcomes.

Future research should focus on longitudinal designs that include objective biomarkers of stress with all-encompassing psychosocial assessment, while taking account of confounding behavioral and genetic variables. Such approaches will better demonstrate the potential causal pathways linking chronic stress and cancer biology. Ultimately, recognizing chronic stress as a legitimate element of cancer pathophysiology may lead to lasting change in preventative medicine, bringing together the divide between mental and physical health, and highlighting the necessity of holistic care in oncology.

References:

1. Murata M. Inflammation and cancer. *Environ Health Prev Med*. 2018;23(1):501. doi:10.1186/s12199-018-0740-1
2. Vignjević Petrinović S, et al. Interplay between stress and cancer: a focus on inflammation. *Front Physiol*. 2023;14:1119095. doi:10.3389/fphys.2023.1119095
3. Feng Z, et al. Chronic restraint stress attenuates p53 function and promotes tumorigenesis. *Proc Natl Acad Sci U S A*. 2012;109(18):7013-7018. doi:10.1073/pnas.1203930109
4. Zong C, et al. Chronic restraint stress promotes gastric epithelial malignant transformation by activating the Akt/p53 signaling pathway via ADRB2. *Oncol Lett*. 2022;24(3):300. doi:10.3892/ol.2022.13420
5. Koh M, et al. Propranolol suppresses gastric cancer cell growth by regulating proliferation and apoptosis. *Gastric Cancer*. 2021;24(5):1037–1049. doi:10.1007/s10120-021-01184-7
6. Lin Q, et al. Effect of chronic restraint stress on human colorectal carcinoma growth in mice. *PLoS One*. 2013;8(4):e61435. doi:10.1371/journal.pone.0061435
7. Weinrib AZ, et al. Diurnal cortisol dysregulation, functional disability, and depression in women with ovarian cancer. *Cancer*. 2010;116(18):4410-4419. doi:10.1002/cncr.25299
8. Rasmuson T, et al. Increased serum cortisol levels are associated with high tumour grade in patients with renal cell carcinoma. *Acta Oncol*. 2001;40(1):83–87. doi:10.1080/02841860175007118.
9. Bernabé DG, et al. Increased plasma and salivary cortisol levels in patients with oral cancer and their association with clinical stage. *J Clin Pathol*. 2012;65(10):934–939. doi:10.1136/jclinpath-2012-200695.
10. Sephton SE, et al. Depression, cortisol, and suppressed cell-mediated immunity in metastatic breast cancer. *Brain Behav Immun*. 2009;23(8):1148-1155. doi:10.1016/j.bbi.2009.07.007
11. Dai S, et al. Chronic stress promotes cancer development. *Front Oncol*. 2020;10:1492. doi:10.3389/fonc.2020.01492
12. Zhang L, et al. Chronic stress-induced immune dysregulation in cancer: implications for initiation, progression, metastasis, and treatment. *Am J Cancer Res*. 2020;10(5):1294–1307.
13. Cole SW, Sood AK. Molecular pathways: beta-adrenergic signaling in cancer. *Clin Cancer Res*. 2012;18(5):1201–1206. doi:10.1158/1078-0432.CCR-11-0641.
14. Dong ZK, et al. Neurobiology of cancer: adrenergic signaling and drug repurposing. *Pharmacol Ther*. 2024;264:108750. doi:10.1016/j.pharmthera.2024.108750.
15. Avogaro A. Diabetes and obesity: The role of stress in the development of cancer. *Endocrine*. 2024;86:48–57. doi:10.1007/s12020-024-03886-1.
16. Antoni MH, et al. The impact of psychosocial stress and stress management on immune responses in patients with cancer. *Cancer*. 2019;125(9):1417-1431. doi:10.1002/cncr.31943
17. Pinquart M, et al. Associations of social networks with cancer mortality: a meta-analysis. *Crit Rev Oncol Hematol*. 2011;75(2):122-137. doi:10.1016/j.critrevonc.2009.06.003
18. Turner-Cobb JM, et al. Social support and salivary cortisol in women with metastatic breast cancer. *Psychosom Med*. 2000;62(3):337-345. doi:10.1097/00006842-200005000-00007
19. Cooper K, Campbell F, Harnan S, Sutton A. Association between stress, depression or anxiety and cancer: rapid review of reviews. *Compr Psychoneuroendocrinol*. 2023;16:100215. doi:10.1016/j.cpnec.2023.100215.
20. Pham AT, et al. Chronic stress related to cancer incidence, including the role of metabolic syndrome components. *Cancers (Basel)*. 2024;16(11):2044. doi:10.3390/cancers16112044
21. Schoemaker MJ, et al. Psychological stress, adverse life events and breast cancer incidence: a cohort investigation in 106,000 women in the United Kingdom. *Breast Cancer Res*. 2016;18:72. doi:10.1186/s13058-016-0733-1
22. Kennedy B, et al. Stress resilience and cancer risk: a nationwide cohort study. *J Epidemiol Community Health*. 2017;71(10):947-953. doi:10.1136/jech-2016-208706