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Review

Heat Shock Proteins in Cancer

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Abstract

Heat shock proteins (HSPs) are vital in the progression of cancer, aiding in the survival, proliferation, and metastasis of tumor cells. The overexpression of particular HSPs, such as HSP70 and HSP27, is often found in various malignancies, including lung, breast, and prostate cancers, and correlates with poor prognosis and enhanced resistance to chemotherapy. These proteins stabilize oncogenic proteins, inhibit apoptosis, and modulate the tumor microenvironment, contributing to cancer aggressiveness. Recent studies highlight the potential of HSPs as biomarkers for predicting cancer prognosis and treatment response. Targeting HSPs with specific inhibitors, notably HSP90 inhibitors, has come forth as a viable therapeutic approach to disrupt cancer-related processes and enhance the effectiveness of chemotherapy treatments. Targeting HSPs offers a multi-targeted approach, as these chaperones stabilize multiple oncogenic proteins simultaneously. Overall, this review aims to provide a comprehensive overview of HSPs in cancer, focusing on their role in tumor progression, their clinical implications as biomarkers and therapeutic targets, and the latest developments in HSP-targeted therapies.

Keywords: HSPs, molecular chaperones, cancer progression, therapeutic targets, cancer biomarkers

1. Introduction

Heat shock proteins (HSPs) represent a well-conserved group within the molecular chaperone family, which is essential for maintaining the cellular homeostasis, especially during stressful conditions. Their significance in cancer research has attracted considerable interest, as they serve both in safeguarding cellular integrity and promoting tumor development. HSPs are classified into several families based on their molecular weight, such as HSP27, HSP40, HSP60, HSP70, and HSP90. Each of these families demonstrates distinct roles and implications in relation to cancer (1). Various stress factors, including increased temperatures, oxidative stress, and interaction with detrimental substances, stimulate the synthesis of HSPs (2). The production of HSPs is crucial for cellular survival under stressful conditions, as they are instrumental in facilitating proper protein folding, preventing aggregation, and helping the degradation of improperly folded proteins. In the context of cancer, increased concentrations of HSPs are often associated with poor prognoses and treatment resistance (3). For example, HSP70 and HSP90 are often elevated in cancers, supporting cell survival by inhibiting apoptosis and promoting proliferation (4).

Recent findings have brought to light the numerous functions of HSPs in cancer development. Specifically, HSPs are vital in fundamental processes such as metastasis, angiogenesis, and the evasion of the immune system (5). The connection between HSPs and the tumor microenvironment is significantly important, underscoring the essential function of HSPs in promoting communication between cancer cells and their neighboring environments (6).

Additionally, HSPs have been recognized as promising biomarkers for the diagnosis and prognosis of cancer. A research has investigated their presence in bodily fluids, including urine and serum, as a non-invasive approach to cancer detection. The rare expression of HSPs in liquid biopsies has resulted in new possibilities for discovering cancer-specific biomarkers; however, the validation of these diagnostic markers is not yet complete. The ability of HSPs to serve as indicators of tumor burden and the effectiveness of treatment underscores their importance in clinical settings (7).

The capacity of HSPs to act as markers for tumor load and treatment efficacy highlights their significance in clinical practice. This method seeks to take advantage of the dependence of cancer cells on survival of heat shock proteins, particularly as traditional therapies frequently encounter challenges due to the protective functions these chaperones provide. The advancement of drugs aimed at targeting HSPs is a dynamic field of research, with numerous compounds presently in the clinical trial phase (8).

Apart from their involvement in the survival mechanisms of cancer cells, HSPs significantly influence the regulation of immune responses. Extracellular HSPs can boost anti-tumor immunity by serving as transporters for peptides derived from tumors, which aids in their presentation to immune cells (9). The immunogenic nature of HSPs has inspired studies into vaccines and immunotherapies based on HSPs, which are designed to exploit the ability of the immune system to determine and exclude malignant cells (10). The association of HSP-peptide complexes with antigen-presenting cells is fundamental for the activation of specific immune responses, illustrating the dual role of HSPs both guardians of tumor cells and catalysts for immune recognition (11).

Moreover, the regulation of HSP expression via epigenetic mechanisms is recognized as a critical component in the field of cancer biology. Epigenetic modifications, such as alterations in histones and DNA methylation, can influence HSP expression levels, which may subsequently affect the characteristics of tumors and the prognostic outcomes for patients. Gaining a deeper understanding of these regulatory pathways could offer valuable insights into the creation of targeted therapies designed to adjust HSP expression in cancerous cells (12).

2. HSPs and Cancer Hallmarks

HSPs are crucial in cancer development because they help stabilize and maintain the function of proteins involved in key cancer traits such as uncontrolled cell growth, avoiding cell death, and spreading to other tissues. When overproduced in tumors, HSPs contribute to cancer progression, making them attractive targets for treatment. Blocking HSP activity can interfere with several cancer-driving pathways, offering new possibilities for cancer therapies and improving the effectiveness of current treatments.

In the case of cancer, HSPs are primarily recognized for their functions in supporting folding, preventing aggregation, and facilitating the removal of incorrectly folded proteins. This role is especially vital in cancer, as cells frequently endure heightened stress levels resulting from rapid growth and adverse microenvironments. Zuo et al. (2024) point out that HSPs are significantly upregulated in cancerous tissues and are intricately linked to the processes of tumor formation and advancement. It is noted that HSPs are pivotal in determining the key characteristics of cancer, as they can either activate or inhibit specific signaling pathways, thus promoting the survival and growth of cancer cells (13).

The levels of HSPs are frequently elevated in response to various stressors, including heat shock, low oxygen conditions, and oxidative stress, which are often found in the tumor microenvironment. In their research, Li et al. (2012) elucidate the role of glucose-regulated protein 78 (GRP78), a HSP family member, in several essential characteristics of cancer. These characteristics include the proliferation of tumor cells, resistance to programmed cell death, evasion of the

immune response, metastasis, and angiogenesis. The authors highlight that GRP78 functions as a stress sensor, adapting to the dynamic conditions of the tumor microenvironment and thus supporting the development of cancerous features (14).

HSPs are crucial to assist in the proper folding of proteins, preventing their aggregation, and enhancing the removal of misfolded proteins. These functions are essential for maintaining cellular integrity under stress such as heat shock, oxidative stress, and nutrient deprivation. In the context of cancer, HSPs are often overexpressed, contributing to the survival and proliferation of malignant cells. This overexpression frequently occurs as a reaction to the tumor microenvironment, which is defined by a range of stressors that cancer cells must manage to survive and grow.

The possibility of employing HSPs as therapeutic targets in the fight against cancer is becoming more widely accepted. Ban et al. (2019) investigated the epigenetic modifications of HSPs within the realm of cancer, proposing that these proteins could serve as potential therapeutic targets as well as diagnostic markers. They highlight that the modulation of HSP expression via epigenetic processes can profoundly influence the behavior of cancer cells, indicating that adjusting HSP levels could modify the characteristics associated with cancer (15).

The concept of HSPs extends into the tumor microenvironment, where they can affect immune responses and facilitate immune evasion, a key characteristic of cancer. In their study, Secli et al. (2021) indicated that extracellular HSPs (eHSPs) can foster the growth and malignancy of cancer cells by promoting processes including angiogenesis and epithelial-to-mesenchymal transition (EMT) (16). These mechanisms are essential for metastasis, as they allow cancer cells to migrate and infiltrate into adjacent tissues. The authors point out that acquiring knowledge about the roles of eHSPs within the tumor microenvironment could facilitate the creation of advanced diagnostic and treatment options for cancer.

Beyond their roles in apoptosis and the tumor microenvironment, HSPs are also vital in metabolic reprogramming, a hallmark of cancer. Avolio et al. (2020) underscore the significance of these metabolic adaptations, which are crucial for cancer cell survival and growth under stress. Specifically, members of the mitochondrial HSP90 family are key regulators of these metabolic pathways, which frequently undergo changes in cancerous cells. The interplay between HSPs and metabolic reprogramming indicates that targeting these proteins could obstruct the metabolic versatility that cancer cells depend on for their development and survival (17).

The investigation into the function of HSPs in immune evasion is an emerging area of research. The tumor microenvironment acts as both a physical barrier for immune cells and a dynamic system that can modify immune responses. According to Becker (2014), solid tumors can foster an immune-permissive environment by utilizing non-transformed host cells (18). HSPs may contribute to this phenomenon by affecting the expression of immune-modulatory factors, thus facilitating the evasion of immune surveillance.

In conclusion, HSPs are crucial in cancer biology, greatly influencing fundamental tumor characteristics like cell survival, proliferation, metastasis, and the evasion of immune responses. Acting as molecular chaperones, HSPs are essential for preserving cellular homeostasis and ensuring that proteins fold correctly, which is critical for the survival of cells under conditions of stress. Their involvement in supporting various hallmarks of cancer, as defined by Hanahan and Weinberg (2011), underscores their importance in tumor development and progression (19). Due to their multifaceted functions, HSPs are promising targets for therapeutic intervention. A deeper understanding of their mechanisms and interactions within the tumor microenvironment is expected to yield valuable insights, potentially leading to more effective cancer treatment strategies. Ongoing research continues to highlight the critical contributions of HSPs to the complex biology of cancer and their potential to improve diagnosis, prognosis, and therapy.

3. Small Heat Shock Proteins (sHSPs)

Small heat shock proteins (sHSPs) constitute a varied group of molecular chaperones essential for preserving cellular proteostasis during different stress conditions. These proteins, generally between 12 to 43 kDa in size, are found throughout all life forms, underscoring their evolutionary importance and functional adaptability (20). The primary function of sHSPs is to prevent the aggregation of

incorrectly folded proteins, which helps to shield cells from the adverse effects of different stressors, including increased temperatures, oxidative stress, and mechanical pressure (21).

The ways in which sHSPs provide their protective mechanisms are complex and varied. For example, they can create large oligomeric complexes with misfolded proteins, thereby sequestering these proteins and inhibiting irreversible aggregation. The ability to bind and stabilize proteins during their unfolding process is crucial, as it helps them to refold later by ATP-dependent chaperone proteins (22). The dynamics of interaction between sHSPs and their substrates are affected by several factors, notably post-translational modifications, which can alter their chaperone function and stability (23).

Studies have shown that sHSPs are not only crucial for the cellular response to heat stress but also have important functions in neurodegenerative disorders. For instance, α-synuclein, a protein involved in Parkinson's disease, shares both structural and functional characteristics with sHSPs, indicating that these chaperones might engage with α-synuclein and influence its aggregation (24). The functions of sHSPs in safeguarding against neurodegeneration are reinforced by evidence demonstrating their increased expression in injured brain tissues, suggesting a possible neuroprotective function (25). In this context, sHSPs such as HSP27 have demonstrated a significant ability to mitigate toxicity induced by α-synuclein, underscoring their potential as therapeutic agents in neurodegenerative diseases (26).

The engagement of sHSPs with various cellular elements highlights their crucial role in sustaining cellular homeostasis. Specifically, in skeletal muscle, sHSPs have demonstrated their ability to safeguard against mechanical stress through interactions with mechanosensitive proteins, thus playing a key role in the regulation of physiological contraction and extension cycles (21). This key role of sHSPs in muscle tissue demonstrates their capacity to adjust to various cellular conditions and stress factors.

In conclusion, small heat shock proteins are crucial in mediating the cellular response to stress in a wide range of biological phenomenon. Their ability to prevent protein aggregation, modulate signaling pathways, and interact with various cellular components positions, making them as vital players in maintaining proteostasis and enhancing cell survival under adverse conditions. Current research related with various functions and regulatory mechanisms of sHSPs is consistently uncovering their importance in both health and disease, highlighting their potential as therapeutic targets for a variety of conditions, such as neurodegenerative diseases and disorders related to stress.

4. HSPs and Cancer

The role of HSPs in cancer is complex and varied. These proteins are recognized for their ability to aid in proper protein folding, inhibit aggregation, and support the breakdown of improperly folded proteins. This assistance is particularly vital for cancer cells, which frequently endure increased proteotoxic stress because of accelerated growth and metabolic imbalances (27). HSP90 has been thoroughly examined and is critical for maintaining the stability and operational integrity of several oncoproteins, especially those linked to cell signaling and proliferation (28).

Studies indicate that HSPs are frequently overexpressed among the different types of cancer, such as breast cancer, lung cancer, and hepatocellular carcinoma. This overexpression plays a significant role in promoting tumor survival, facilitating metastasis, and enhancing resistance to treatment (29). In the context of non-small cell lung cancer, the presence of HSPs has been correlated with drug resistance, attributed to their capacity to alter apoptotic pathways and facilitate cell survival when subjected to chemotherapy (30).

Additionally, HSPs are being recognized as promising diagnostic and prognostic markers for cancer assessment. Their abnormal expressions in tumor tissues and bodily fluids have been associated with the advancement of the disease and the outcomes for patients (31).

The therapeutic approach of targeting HSPs has seen increased interest in recent years. Inhibitors of HSP90, including geldanamycin, have exhibited potential in both preclinical and clinical environments by interfering with the chaperoning of various oncogenic proteins, ultimately resulting in the death of cancer cells. Furthermore, the suppression of HSF1, which is a transcription

factor controlling the expression of HSPs, has been suggested as an innovative approach for cancer therapy.

The extracellular roles of HSPs are receiving increasing focus. Recent research has shown that cancer cells can secrete HSPs, which may influence the tumor microenvironment, enhance angiogenesis, and accelerate metastasis. The extracellular activity of HSPs points to their potential as therapeutic targets and biomarkers, thus unlocking new frontiers for the treatment and monitoring of cancer.

4.1. HSPs in Breast Cancer

HSPs, particularly HSP70, HSP90, and HSP27, are often observed to be overexpressed across many types of cancer, including breast cancer. This overexpression is often correlated with more aggressive tumor characteristics and worse prognosis. For instance, while HSP70 is normally present in healthy cells, its expression becomes dysregulated in numerous tumor cells, contributing to their survival in stressful environments (32). The enhanced expression of these proteins is linked to the capacity of cancer cells to avoid apoptosis, a defining characteristic of cancer advancement. HSPs, as they help ensure proteins fold correctly, prevent their aggregation, and promote the elimination of misfolded proteins.

The role of HSPs in breast cancer is underscored by their engagement with critical signaling pathways. Significantly, HSP90 has been proven to interact with steroid receptors and multiple signaling proteins, which has directed research towards the formulation of therapies that specifically target HSP in the context of breast cancer (33). This interaction highlights the promise of HSPs as focal points for therapy, since blocking their activity may interfere with the signaling mechanisms that facilitate proliferation and persistence of tumors.

The regulation of HSPs is influenced by multiple factors, notably heat shock factor 1 (HSF1), which serves as a significant regulator to the heat shock response. Besides its function in regulating HSP expression, HSF1 has been linked to the enhancement of the cancer stem cell (CSC) phenotypic characteristics in breast cancer. Increased expression levels of HSF1 are associated with poor prognoses in breast cancer patients, suggesting that HSF1-driven mechanisms may contribute to heightened tumor aggressiveness and treatment resistance (34). This suggests that focusing on HSF1 may be an effective approach to disrupting the cancer stem cell phenotype and enhancing the efficacy of existing therapies.

The participation of HSPs in drug resistance represents a significant dimension of their function in breast cancer. Research indicates that HSPs can enable cancer cells to resist a range of chemotherapeutic drugs by shielding them from apoptosis triggered by these medications. Specifically, HSP27 and HSP70 have been linked to the emergence of resistance to cancer treatments, positioning them as promising targets for combination therapy approaches (35). The integration of HSP inhibitors with standard chemotherapy has demonstrated potential in preclinical research, indicating that these approaches may improve treatment effectiveness by addressing resistance mechanisms (36).

Beyond their functions within cells, HSPs have been identified as being released by cancer cells through exosomes. This secretion can affect the tumor microenvironment and modulate the immune responses. The presence of these extracellular HSPs may act as indicators of cancer advancement and treatment efficacy, underscoring their promising role in theranostics (37).

Recent transcriptomic research has revealed that specific HSP genes exhibit dysregulation across different molecular subtypes of breast cancer. This observation suggests that the expression patterns of HSPs could be utilized to classify breast cancer subtypes and predict patient outcomes. For instance, in a study discovered both shared and distinct HSP genes linked to overall survival, underscoring their potential as prognostic biomarkers (38). These results emphasize the significance of comprehension of the distinct roles of HSPs in various breast cancer subtypes, which may inform the creation of personalized treatment approaches.

In conclusion, HSPs have various important functions in breast cancer, affecting tumor development, resistance to treatment, and overall patient prognosis. Their participation in vital cellular mechanisms and signaling pathways put forward them as potential targets for therapeutic strategies.

4.2. HSPs in Lung Cancer

The expression of HSPs in lung cancer has attracted considerable interest because of their roles in tumor development, progression, and therapeutic response. This article seeks to examine the diverse functions of HSPs in lung cancer, referencing various studies that underscore their significance in cancer biology and treatment strategies.

The presence of high-molecular-weight (HMW) HSPs, particularly HSP-60 and HSP-70, has been identified in lung carcinoma through immunohistochemical methods. In a research study done by Michils (2001), a quantitative analysis was undertaken to evaluate the concentrations of (HMW and low-molecular-weight (LMW) HSPs in lung tissues, distinguishing between tumor and non-tumor samples. The results indicated that tumor tissues had markedly elevated levels of HSP-60 and HSP-70 when contrasted with healthy lung tissues, implying that these proteins may function in the malignant transformation and persistence of lung cancer cells (39). The elevated levels of HSPs in tumor tissues suggest their potential utility as biomarkers for diagnosing and predicting lung cancer outcomes.

The function of HSPs goes beyond simply their expression levels; they are also involved in the processes that contribute to drug resistance in lung cancer. Xia et al. (2021) conducted a review on the role of GRP78, a HSP family member, in lung cancer. GRP78 serves as a key stress sensor within the endoplasmic reticulum (ER), facilitating the ER stress responses that are vital for the survival of cancer cells in challenging environments. The findings highlight that GRP78 is frequently overexpressed in tumors and correlates with unfavorable outcomes for patients with lung cancer (40). This indicates that focusing on GRP78 may improve the effectiveness of current treatments by addressing resistance mechanisms.

Beyond their involvement in drug resistance, HSPs play key roles in multiple cellular processes that facilitate tumor progression. A study done by Ferreira et al. (2019) emphasizes the importance of immune-based prognostic biomarkers in lung cancer, indicating that the expression levels of specific HSPs may be associated with immune responses and the effectiveness of treatments (41). The connection between HSP expression and the immune microenvironment may offer valuable understanding of how lung cancer cells avoid detection by the immune system, thus promoting tumor development and spread.

Recent studies have investigated the connection between HSPs and alternative splicing in lung cancer. Awad and El-Hadidi (2021) examine how alternative splicing can produce different isoforms of HSPs, each potentially serving unique roles in the biology of cancer (42). This complexity introduces an additional dimension to our comprehension of HSPs in lung cancer, as various isoforms may have the potential to affect tumor characteristics and treatment responses.

The participation of HSPs in lung cancer is evident in the field of immunotherapy. Herbst (2019) highlights the progress made in cancer immunotherapy, especially regarding immune checkpoint inhibitors, and observes that the expression levels of HSPs could act as predictive biomarkers for assessing treatment efficacy (43). The capacity of HSPs to influence immune responses indicates that they may be utilized to improve the efficacy of immunotherapeutic approaches in lung cancer patients.

In conclusion, HSPs play a crucial role in the biology of lung cancer, affecting tumor development, resistance to treatment, and the capability to escape the immune system's response. Their increased presence in tumor tissues, correlation with unfavorable outcomes, and potential as targets for therapy emphasize the significance of HSPs in lung cancer studies. As investigations related with the functions of HSPs advances, they may provide new opportunities for therapeutic approaches and tailored treatment plans in the management of lung cancer.

4.3. HSPs in Colorectal Cancer

Colorectal cancer (CRC) represents a major health worldwide issue, ranking among the foremost causes of cancer-related illness and deaths. The pathogenesis of CRC is complex, involving multiple molecular mechanisms, with HSPs identified as key contributors. HSPs that support the folding, stabilization, and degradation of proteins, particularly in reaction to stressful situations. Their involvement in cancer biology, particularly

in CRC, has attracted growing interest due to their significant roles in tumor advancement, metastasis, and resistance to treatment.

HSPs are recognized for their elevated expression in multiple types of cancer, particularly CRC, where they play significant roles in tumor development and advancement. Javid et al. (2022) emphasized that various HSPs, such as HSP27, HSP40, HSP60, HSP70, HSP90, and HSP110, possess anti-apoptotic characteristics and are integral to mechanisms like tumor cell growth, invasion, and metastasis (44). This points to the potential role of HSPs as biomarkers to diagnose and prognose of CRC, since their expression levels are linked to the severity of the disease and the resulting patient outcomes.

The function of HSPs in CRC is complex and diverse. Buttacavoli et al. (2021) utilized a multi-omics strategy to explore the expression patterns of HSPs in breast cancer that may also be relevant to CRC due to the common pathways involved in tumor development (45). The involvement of HSPs in influencing the tumor microenvironment represents a significant aspect of their role in CRC. According to Lang et al. (2019), increased concentrations of HSPs within tumor cells correlate with unfavorable survival rates since they promote intrinsic characteristics of tumor cells, including unchecked growth and heightened metastatic capabilities (46).

Beyond their involvement in tumor biology, HSPs have also been linked to the emergence of resistance to cancer treatments. Zhang et al. (2020) examine the ways in which HSPs can affect tumor growth and metastasis, emphasizing their dual roles in cancer progression (47).

Additionally, the extracellular roles of heat shock proteins (HSPs) have attracted interest regarding their involvement in immune evasion and tumor advancement. Taha et al. (2019) investigated the capacity of extracellular HSPs to function as alarmins, affecting immune responses and possibly aiding tumor cells in resisting destruction by the immune system (48).

4.4. HSPs in Hepatocellular Carcinoma

Hepatocellular carcinoma (HCC) is the most frequent type of primary liver cancer. HSPs have been found to function in tumor development, metastasis, and resistance to treatment of HCC.

In HCC, the levels of several HSPs, including HSP27, HSP70, and HSP90, are frequently elevated, leading cancer cells to thrive under adverse conditions. For example, HSP70 has been associated with increased chemoresistance of HCC cells. Wang et al. (2021) indicated that incomplete radiofrequency ablation (iRFA) resulted in the upregulation of HSP70, which inhibited pyroptosis and allowed transformed cells to survive, thus enhancing chemoresistance (49).

The involvement of HSPs in the progression of HCC is further validated by their association with various oncogenic processes. As noted by Paul et al. (2024), HSPs are instrumental in regulating the cell cycle, apoptosis, and cellular proliferation, which are all critical components in cancer development (50). Specifically, HSP27 has been identified as a vital element in inhibiting apoptosis in HCC, thereby facilitating tumor growth and metastasis (51). This underscores the dual function of HSPs in enhancing cancer cell survival while also contributing to the aggressive characteristics of HCC.

5. Therapeutic strategies of HSPs

HSPs are key molecules for cellular stress response and are involved in numerous diseases, including cancer, neurodegenerative illnesses, and cardiovascular ailments. Functioning as molecular chaperones, they aid in the correct folding of proteins, prevent their aggregation, and promote the degradation of improperly folded proteins. Given their importance in sustaining cellular homeostasis, HSPs are receiving heightened attention as potential candidates for therapeutic targeting and as biomarkers.

In the context of cancer treatment, HSPs hold particular importance. HSP70 and HSP90 are frequently found to be overexpressed in cancer cells, which contributes to tumor progression and resistance to chemotherapy. The resistance encountered with ABL-tyrosine kinase inhibitors (TKIs) in chronic myeloid leukemia (CML) demonstrates the critical requirement for novel strategies to effectively overcome this obstacle. Research indicates that leukemia stem cells and the genetic variability in CML pathogenesis suggest

that targeting HSPs may improve the effectiveness of therapy (52).

HSPs play a role in ischemic heart disease and a range of cardiovascular conditions, alongside their link to cancer. Sueta et al. (2019) highlight the difficulties associated with antithrombotic treatment in cancer patients, pointing out that HSPs affect the management of therapy in individuals who have both malignancies and cardiovascular issues. This situation calls for a collaborative, multidisciplinary strategy to enhance patient care (53).

Digital health interventions broaden the scope of therapies related to health service providers. Kraft et al. (2021) examined the eHealth platform eSano, which offered internet and mobile-based solutions for mental and behavioral health issues. Incorporating HSPs-centered content into these platforms could improve patient engagement and compliance with treatment plans (54).

Additionally, healthcare safety professionals contribute to fostering a culture of safety within healthcare environments. Le et al. (2024) advocated for systematic reviews which aimed to identifying interventions that enhance safety culture, especially in the field of oncology. Gaining insights into how HSPs influence cellular stress responses may lead to the improvement of safety protocols and training initiatives, ultimately benefiting patient outcomes (55).

6. Conclusion

HSPs are essential components in the development of cancer, as they enhance the survival, growth, metastasis, and ability of tumor cells to evade the immune system. Their overexpression contributes to resistance against cell death and alters the tumor microenvironment, making them key factors in the advancement of cancer and the resistance to cancer treatment.

HSPs show promise as non-invasive biomarkers for cancer diagnosis, prognosis, and treatment monitoring, with their levels correlating to clinical outcomes across different cancers. Therapeutically, targeting HSPs -especially with HSP90 inhibitors- offers a multi-targeted approach by disrupting several oncogenic proteins simultaneously. Additionally, HSPs' role in immune regulation has spurred the development of HSP-based vaccines and immunotherapies.

Epigenetic control of HSP expression adds complexity but also presents new opportunities for targeted cancer treatments. Ongoing research about HSP functions within tumors is crucial for advancing cancer diagnosis and therapy.

In summary, HSPs are active drivers of cancer progression and valuable targets in diagnosis and treatment. Continued study on this subject is likely to improve patient outcomes.

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