THE SCIENCE WORLD
A Monthly e Magazine
ISSN:2583-2212
April, 2023; 3(04), 473-479

Popular Article

Immunosuppression and Cancer

Suruchi Sharma*[1] And Sahil Sharma[2]
[1]M.V.Sc. Veterinary Biochemistry DGCN COVAS, CSKHPKV, Palampur
[2]M.V.Sc. Animal Nutrition DGCN COVAS, CSKHPKV, Palampur
https://doi.org/10.5281/zenodo.7808536

Abstract

Cancer is defined as an unregulated and abnormal cell proliferation that has been around since around 120,000 years ago. Its uncontrolled development is caused by the cell mechanism degrading as a result of chemical, radiation, or genetic causes. Our bodies' immune systems aid them in fighting off cancer cells that spread unchecked and harm other tissues. The immune system's reaction to antigens can, however, occasionally be suppressed. In some surgical procedures, such as transplantation, immunosuppression can be created by the use of medications or triggered by biological processes. Due to the suppression of cancer and the inability of the immune system to fully express the reaction, certain cancers are tolerated by the immune system while others do not receive any protection. In this scenario, the question is whether the immune system's response mechanism can be identified by utilizing immunosuppressive medicines in this manner.

Keywords: adaptive immunity, cancer, immunosuppression, innate immunity

Introduction

The World Health Organization (WHO) and the American Cancer Society (ACS) database provided data for 2018 showing that there were roughly 22.4 percent male and 18.2 percent female cancer patients in the 0-74 age range. The three most prevalent malignancies in 2018 are lung cancer (2.09 million cases), breast cancer (2.09 million cases), and prostate cancer (1.28 million cases). The most fatal malignancies are those of the lung, liver, and stomach. Major cancer types were chosen, with lungs, breast, colorectal, stomach, prostate, and liver accounting for around 55% of the global incidence in 2012. Even though the precise process by which cancer develops is unknown, it is

understood that the cells that require apoptosis continue to proliferate uncontrollably and more quickly. Human genome project data suggests that cancer is genetically inherited and is characterised by mutations. Similar to how it works with any disease, the immune system has tight interactions with tumours throughout the entire cancer phase. Cancer cells and immune cells coexist in a relationship that both inhibits and encourages the formation of tumours. This trait is currently thought of as a differentiating trait. Cancer's traits were first recognised in 2000. The continuation of proliferative signalling, resistance to cell death, avoidance of immunosuppression, and activation of invasion and metastasis are all dependent on these traits. In 2011, two crucial features were added in addition to these features. Two of them include reprogramming energy metabolism and guarding against immune system deterioration. Cancer is distinguished by immunosuppressive T lymphocytes, which offer promise for treatment by eradicating cancerous cells. The immune system's capacity to either promote or treat cancer is related to immunosuppression. Immunosuppressive medications and other techniques have been applied in animal experiments to establish a particular immunological state. With epithelial-induced cancer making approximately 75% of the cases, immunosuppressive medications have only recently been used to diagnose cancer. Pediatric children with all of these issues are unable to grow and develop normally due to immunosuppressive medications. Prednisone, azathioprine, and cyclosporin A are all used together as part of the current immunosuppressive therapy paradigm. Excessive stress is also known to harm the immune system and cause cancer. Noradrenaline and adrenergic receptors have been shown to have an impact on tumour cells, and psychosocial stressors have a direct impact on the formation of tumours, according to research by psycho-immunologists. A ray of hope in the fight against cancer is immunotherapy, which was created by turning off the immunity mechanisms. In many situations, immunotherapy has already taken the place of conventional cancer therapies. Because that return rates for tumours range from 20 to 80%, it was not regarded as a curative treatment for all malignancies, although there has been significant advancement as long as a return occurs (Yurkeli and Erbas, 2021).

Cancer

The unchecked proliferation of cells with aberrant growth traits is referred to as cancer. It can be brought on by bacteria, viruses, radiation, inheritance, environmental factors, eating habits, and chemicals, among other things. According to studies, the dynamic alterations in the genome play a role in the development of cancer. There are two types of tumor cells: benign and malignant. The

Official Website
www.thescienceworld.net
thescienceworldmagazine@gmail.com
Published 07.04.2023

fact that benign tumors are localized to the location in which they are located defines them. Malignant tumours can infect lymph tissue or blood arteries in addition to the location in which they are detected. There are various phases in the genesis of cancer, and four to seven age-related stochastic malignancies have been identified in the human population. Cancer produced by external factors is more frequent than cancer that is inherited. Predisposition is brought on by the hereditary transmission of the problem in suppressing genes that control tumour formation and the make-up of environmental factors. Point mutations and other minor alterations appear to cause observable degradation in tumour cells. Researchers are still examining if certain diseases are predisposed to by genes. Although being genetically passed down from our ancestors, cancer has emerged as one of the most prevalent diseases of the modern period due to the impact of numerous environmental variables. The metabolism of cancer cells must be rearranged for them to develop and proliferate. The effect of changed metabolism is an increase in glucose consumption and lactate fermentation. This process goes on in the presence of mitochondria. It can be explained by the propensity of malignancy to glucose. This occurrence is known as the "Warburg Effect." For the past ten years, additional research has been done on this occurrence, which has been well-known for more than 90 years. The activation of cancer cells' immune defence mechanisms and immunosuppressive networks is greatly aided by tumour glycolysis. Current research has demonstrated that anti-tumor cells are effective against cancer cells. It is believed that metabolism and immune evasion are interdependently involved in the progression of cancer during metabolic reprogramming.

Immune system and Cancer

Immune defenses are employed by the body against antigens. Many proteins and cells make up the immune system. Innate immunity and acquired immunity are the two categories. Innate immunity is responsible for the initial evolution of the immune system. Humoral immunity and cellular immunity are the two subtypes of acquired immunity. In cellular immunity, the body fights intracellular antigens, whereas humoral immunity engages antigens outside the cell. The immune system eliminates cancerous cells before they develop into a threat. This condition is known as cancer immuno-surveillance. To achieve this, regular cell homeostasis and carcinogenesis inhibition are used. Tumor cells are no longer passive targets for the immune system, according to immune surveillance theory. Studies show that the suppression of the immune system has resulted in some circumstances, cancer. These two features of the immune system led to the creation of the phrase

Official Website
www.thescienceworld.net
thescienceworldmagazine@gmail.com
Published 07.04.2023

"immune regulation." The term "cancer immuno-surveillance" is abbreviated as 3E. The stages of these processes include elimination, equilibrium, and escape. If the tumour cell progresses through these stages, it will grow. NK cells, a key component of the immune system's immunological surveillance, are very significant. Effector lymphocytes called NK cells assist in the elimination of malignancies. They can accomplish this via interacting with and enhancing immune responses, using cytolytic granules and death receptors, inducing the generation of cytokines, and employing cytolytic granules and death receptors. NK cells have been demonstrated to exhibit leukaemia activity against the vaccination in the context of hematopoietic stem cell transplantation, and they are crucial to the therapeutic effectiveness of antibodies. Yet, tumour cells have a higher expression of adaptive immune components such CD4 + auxiliary T cells, CD8 + cytotoxic T cells, and antibodies. T cells that are efficient and successfully get through the endothelial barrier are directed to the tumour stroma rather than the target tumour cell. Immunosuppressive signals could very well be present here. At this stage, tumour cells may be completely eliminated, and clonal variations may appear. Clonal variations act immune-suppressively to decrease their immunogenic characteristics and increase resistance. These events provide a description of the immunoediting theory. Since the earliest stages of carcinogenesis, the immune system and tumour have been interacting and changing one another. Either one side wins in this process, or it becomes chronic and the equilibrium lasts for years. The most frequent cause of cancer in those with immunodeficiency is viruses. There have been reports of malignancies connected to the human papillomavirus (HPV), Kaposi's sarcoma-associated herpesvirus (KSHV), and lymphomas connected to the Epstein-Barr virus (EBV).

Natural immunity to cancer

The body's initial line of defence against any antigen is natural immunity. Natural killer cells (NK), neutrophils, and macrophages are examples of innate immune cells. These cells work in conjunction with T cells. Oncological viruses also influence normal immunity, rendering the tumour site unprotected. The development of tumours is inhibited by natural immunological cells, according to extensive research on cancer immunity. It has been established that lymphocytes that express antigen receptors and the recombination activating gene 2 (RAG-2) are essential for the immunosuppression of cancer. Mice lacking RAG-2 have been found to be unable to reorganize lymphocyte antigen receptors. Natural killer T (NKT) and NK cells take involvement in cancer immunosurveillance as well.

Official Website
www.thescienceworld.net
thescienceworldmagazine@gmail.com
Published 07.04.2023

Adaptive immunity and cancer

Signals of danger can be detected by the immune response's kinetics. The adaptive immune system can be strengthened when a signal of risk is received. By administering cyclophosphamide and fludarabine to T cells, it was possible to detect the adaptive immune system's beneficial effects on chemotherapy. An ongoing interaction exists between innate and acquired immunity. Adaptive immunity has been demonstrated to be suppressed by inflammatory stimuli, even if immunotherapy is anticipated to increase this synergy.

Immunosuppressive mechanisms

A hormone based on steroids called glucocorticoids is used to treat both acute and chronic disorders. It is the anti-inflammatory, immunosuppressive, and anti-allergic drug that is administered the most frequently. Recent research has shown that the immunosuppressive effect of glucocorticoids may be mediated via the release of target cells from leukocytes. Yet, immunosuppressive mechanisms function as a result of immunological modifications brought on by surgical operations, and in this instance, glucocorticoid release takes place. Nerve end releases of adrenaline and noradrenaline also depress the immune system. When these effects interact with immune cell receptors, immunosuppression results.

Interleukin-1 and TGF-beta, which are released by tumours into the fluid of tumour cysts, have been found to be effective at reducing lymphocyte activation. There are recognized impacts of glioblastoma on the microenvironment's immune response. There is a propensity for modulator use to prevent immunosuppression.

Cancer immunotherapy

With the advancement of technology, cancer therapy has improved recently. Currently utilized therapies include chemotherapy, surgery, radiation therapy, and immunotherapy, but no permanent cure has yet been found. The immune system is strengthened by the cancer-fighting therapy known as immunotherapy. By binding to cancer cells and inhibiting particular proteins (immune control points), monoclonal antibodies alter therapeutic tactics and halt uncontrolled proliferation of cancer cells. Despite this, not every patient saw success. Due to T cells' function in signaling, anti-tumor immunity is reduced as a method. The CTLA-4 ligand reduces T-cell responsiveness by inhibiting activating signals. It functions as a regulatory T-cell as well. The anti-

Official Website
www.thescienceworld.net
thescienceworldmagazine@gmail.com
Published 07.04.2023

tumor effects are stopped as a result. At this point, immune suppressive agents are used to create an immunotherapeutic therapy procedure. There are three different categories of immunotherapeutic antigens that elicit an immune response against tumours. These include cancer-testis antigens, antigens associated to tumours, and tumor-mutated antigens. Different tumour tissues express tumor-related and cancer-testis antigens in different ways. These cells were able to respond to their own antigens in autoimmunity by reducing central tolerance. Effects from antigen expression in healthy tissues have been observed. Neo-antigens, or tumor-mutated antigens, arise through somatic mutation and are tumor-specific. The most promising immunotherapy targets are these antigens. The emergence of next-generation sequencing (NGS) technology has made it possible to search the genome for neo-antigens. In studies on the immune system's function in cancer, T cells are crucial. T cells with anti-CTLA-4, anti-PD-1, and anti-PD-L1 antibodies identify the control mechanism (programmed death-ligand 1). The most recent clinical trial of immune checkpoint treatment, which included blocking antibodies against cytotoxic T cells against PD-1 programmed to CTLA-4, was successful. It was discovered that these activities caused the death and modification of cancer cells (Yurkeli and Erbas, 2021).

Immunosuppressive drugs and cancer

During transplant surgery, immunosuppressive medications are frequently used to suppress immunity permanently or until the body takes the organ into the tissue. At the same time, it's crucial to comprehend how immunosuppressive medications affect the immune system in order to treat immunological illnesses. Cyclophosphamide is an effective immunosuppressive medication, as an example. It is frequently employed in bone marrow and blood transplantation. It was created to target the cancer cell, however it was discovered to be ineffective against the phosphamidases of the cancer cell. Aldehyde dehydrogenase has been discovered to have effects on a variety of cellular expressions, the anti-cancer therapeutic index of cyclophosphamide, and immunosuppressive qualities. Cancer-associated fibroblasts (CAFs) are typically the most noticeable elements of the microenvironment in the form of solid tumours. It is well recognized that tumour cell development stimulates angiogenesis, which fuels inflammation and promotes malignancy. In addition to the inflammatory microenvironment, tumours have a tendency to evade the immune system and suppress the immune system. By modifying the microenvironment around the tumour, CAFs influence immune control. They enter tumours to obtain immune cells. A paucity of T-cell infiltration in the

Official Website
www.thescienceworld.net
thescienceworldmagazine@gmail.com
Published 07.04.2023

tumour microenvironment in cancer patients with reduced immune cytotoxicity suggests negative implications. Moreover, prednisone, ATG (Anti-Thymocyte globulin), and azathioprine—all immunosuppressive drugs—accelerated metastases in mice. This leads to the hypothesis that immunosuppression promotes the growth and spread of tumours that were previously underdeveloped.

Conclusion

The immune system's ability to be suppressed by immunosuppressive drugs is done so through cellular and molecular pathways. Due to the presence of suppressive cells and secretions in the tumour microenvironment, the immune system in cancer disease is unable to completely carry out its functions. Despite the fact that the processes seem to support the anti-tumor property, they have a negative impact on cancer treatment by creating a favorable environment for tumour development. This adverse impact may cause patients to unexpectedly pass away while pretending to be recuperating. Recent studies have demonstrated the potential of immunotherapeutic strategies and immune-suppressing agents in the treatment of cancer. Current research focuses on immunological development against oncological viruses and immuno-cancer vaccines. Chemo preventive and control agents are non-toxic substances that reduce or completely remove immunosuppression in the tumour microenvironment. These substances will aid in the development of treatment plans and the understanding of how cancers resist therapy.

References

A Yurekli and O Erbas. Cancer and Immunosuppression, Journal of Experimental and Basic Medical Sciences, (2021) vol 2(2): pp 116-121

Official Website
www.thescienceworld.net
thescienceworldmagazine@gmail.com

Published 07.04.2023