Proceedings of the 5th International Conference on Biological Engineering and Medical Science
DOI: 10.54254/2753-8818/96/2025.21969

The Role of IL-10 in Regulating Inflammatory Pathways and Cancer Risk

Yuwei Ouyang

Edmonds Community College, Lynwood, the United States
Ouyang_yw@outlook.com

Abstract: Interleukin-10 (IL-10) is an important anti-inflammatory cytokine that plays a crucial role in regulating immune responses by preventing the immune system from overreacting. It maintains immune homeostasis by suppressing the production of pro-inflammatory cytokines, thus reducing excessive inflammation. This paper explores the genetic variations and biological mechanisms associated with IL-10, focusing on how these factors influence cancer risk and tumor development. Research from genetics, cell biology, and clinical studies reveals that IL-10 has complex, dual roles in cancer. IL-10 plays a dual role in cancer biology, it mitigates chronic inflammation, potentially decreasing the likelihood of DNA damage and tumorigenesis. Conversely, IL-10 may foster an immunosuppressive milieu that enables tumor cells to escape immune surveillance, thus facilitating cancer advancement under specific circumstances. These paradoxical functions highlight IL-10's significance in both cancer prevention and progression. The findings suggest that IL-10 could serve as a valuable therapeutic target for cancer treatment and as a biomarker for identifying inflammation-related cancers. Understanding IL-10's dual roles not only provides new insights into the mechanisms of cancer development but also underscores its potential in developing innovative cancer therapies and improving immune system regulation.

Keywords: IL-10, inflammation, cancer risk, genetic polymorphisms, tumor microenvironment

1. Introduction

Interleukin-10 (IL-10) is a key cytokine that helps keep your immune system balanced. It helps control inflammation, ensuring that your immune system responds in a healthy way.IL-10 is made by different types of immune cells, such as T cells, B cells, macrophages, and dendritic cells. Its main job is to stop other proteins (called "cytokines") that make our immune system too active. Some of these cytokines are IL-6, IL-12, and TNF-α. Too much of these cytokines can cause tissue damage during infections or long-lasting inflammation.Chronic inflammation has been shown to play a role in causing various cancers, like colorectal, liver, and gastric cancers. This makes IL-10 an important part of how tumors grow. [1-3] IL-10 works by attaching to a specific receptor, IL-10R, which activates certain pathways like the JAK-STAT pathway. This process reduces the production of pro-inflammatory cytokines, controls the activity of immune cells, and helps keep the immune system balanced.[2]Certain genetic polymorphisms in the IL-10 gene, such as rs1800896, have been linked to an increased risk of diseases, including rheumatoid arthritis, inflammatory bowel disease, and

© 2025 The Authors. This is an open access article distributed under the terms of the Creative Commons Attribution License 4.0 (https://creativecommons.org/licenses/by/4.0/).

DOI: 10.54254/2753-8818/96/2025.21969

various cancers like prostate cancer.[3] These polymorphisms can affect IL-10 production levels, altering the body's inflammatory response. However, the exact mechanisms underlying these associations remain unclear, and further research is needed to determine how these genetic variations influence IL-10 expression and function.

IL-10 has a dual role: it can suppress harmful inflammation, which reduces the risk of cancer by limiting tissue damage from chronic inflammation. This tissue damage can lead to genetic mutations and tumor initiation [1,4]. However, in certain situations, IL-10 can also create an environment that suppresses the immune system, allowing cancer cells to hide from detection. High IL-10 levels can stop the activity of certain immune cells, which can help tumors grow undetected. [1,4]

It's important to understand this because it helps us develop effective treatments that can control inflammation and also help the immune system fight cancer. [5,6] To do this, we might need to change IL-10 levels to get the right balance between controlling inflammation and keeping the immune system strong. This shows that IL-10 is important not only in preventing cancer but also in helping it grow. This makes IL-10 a good target for future cancer treatments.

2. Genetic Polymorphisms of IL-10 and Cancer Risk

Gene variations can make some people more likely to get cancer than others. One of these variations, called rs1800896, is particularly interesting because it has been studied a lot. It is linked to a lower amount of a protein called IL-10, which helps control inflammation in the body. Inflammation has the potential to contribute to cancer development by fostering an environment conducive to cellular mutations, promoting unchecked cellular proliferation, and facilitating tumorigenesis. [3][6] Studies have shown that people with the rs1800896 variant are more likely to get aggressive cancers, including prostate cancer, where the inflammation helps tumors grow and spread. [3]

There are other variations in the IL-10 gene besides rs1800896. These variations, called rs1800871 and rs1800872, can affect how much of the IL-10 protein is produced. This can reduce the anti-inflammatory effect of the IL-10 protein. Studies have found that people with low IL-10 expression due to these changes in their genes may have a higher risk of cancers like gastric, lung, and colorectal cancers. In these cancers, long-lasting inflammation can play a key role in the development of cancer.

IL-10 interacts with other genes involved in inflammatory responses, such as Toll-like receptor 4 (TLR4), highlighting its role within a complex genetic network that influences cancer risk. [3][6] TLR4 plays a crucial role in recognizing pathogens and initiating immune responses, and its genetic variations can affect inflammatory pathways. When IL-10 and TLR4 gene variations are together, they can make inflammation worse, increasing the chance of ongoing inflammation and cancer. Studies show that IL-10 gene variations not only change how much of a protein called cytokine there is in the body but also change how the immune system responds to tumors. This can affect how well tumors start and grow. In addition to genetics, the environment can interact with IL-10 gene variations, further changing cancer risk. Lifestyle choices like smoking, poor diet, obesity, and chronic infections can trigger inflammatory responses, which may not be regulated well in people with IL-10 gene variants. For example, smoking has been shown to amplify inflammation in people with low IL-10 expression, increasing the risk of lung and bladder cancers. Similarly, having a certain version of the IL-10 gene and a stomach infection with Helicobacter pylori can significantly raise the risk of getting gastric cancer.

Carcinogens, such as environmental toxins, industrial chemicals, and radiation, can interact with IL-10 gene variations. These exposures may cause DNA damage and oxidative stress, leading to chronic inflammation that lasts because IL-10 doesn't regulate it well. This ongoing inflammatory state creates an environment where cancer can develop, especially in people who are genetically

DOI: 10.54254/2753-8818/96/2025.21969

susceptible. It's important to understand how a person's genes and the environment affect their risk of cancer. [5]

Knowing who has IL-10 gene variations can help predict who might get certain cancers, which can help create treatments that work better for each person. Also, genetic screening can help create personalized treatments by using a person's genes and the environmental risks they face. This can help improve how well we can prevent, detect, and treat cancer.

3. How IL-10 Works in the Body

IL-10 is a hormone that helps the immune system fight off infections. It does this by attaching to a receptor called IL-10R, which is found on different types of immune cells like monocytes, macrophages, and dendritic cells. IL-10 also works with certain types of T and B lymphocytes. [2] The IL-10 receptor (IL-10R) comprises two subunits, IL-10R1 and IL-10R2. IL-10R1 is primarily involved in the binding of interleukin-10 (IL-10), while IL-10R2 plays a crucial role in signal transduction. Upon IL-10 binding, the receptor activates the Janus kinase (JAK) and signal transducer and activator of transcription 3 (STAT3) signaling cascades. This activation triggers a series of events that suppress pro-inflammatory cytokines, such as IL-6, IL-12, TNF-α, and IFN-γ. This prevents excessive immune activation and maintains immune balance.

Animal studies, particularly those using IL-10 knockout mice, have provided valuable insights into IL-10's protective role against hyperactive immune responses. In these models, the absence of IL-10 leads to uncontrolled inflammation, with high levels of pro-inflammatory cytokines and widespread tissue damage. IL-10-deficient mice develop inflammatory diseases, such as colitis, arthritis, and symptoms similar to systemic lupus erythematosus. This demonstrates IL-10's crucial role in controlling immune responses. [1,4] These findings show that IL-10 is like a brake on the immune system, keeping it from going too far and causing problems like chronic inflammation and autoimmunity.

IL-10 significantly impacts immune regulation beyond cytokine suppression. It is crucial for the differentiation and function of regulatory T cells (Tregs), which are vital for immune tolerance and the prevention of autoimmune disorders. IL-10 enhances Treg suppressive functions, effectively managing inflammatory responses. Additionally, it modulates antigen-presenting cells (APCs), such as dendritic cells and macrophages, by downregulating MHC class II and co-stimulatory molecule expression, thereby limiting T cell activation and further regulating immune responses. IL-10 also inhibits inflammatory signaling pathways, notably the NF-κB pathway, a central regulator of inflammation. By blocking NF-κB activation, IL-10 decreases the transcription of pro-inflammatory genes, reducing the production of inflammatory mediators.

All of these mechanisms show how important IL-10 is in keeping the immune system balanced, preventing ongoing inflammation, and protecting against autoimmune diseases.[4] It's crucial to understand IL-10's regulatory functions to develop treatments that can adjust immune responses in cases of inflammation and autoimmune disorders, as well as in cancer.

4. IL-10's Double Role in Cancer

Interleukin-10 (IL-10) has a complicated and situation-specific role in cancer. Depending on the biological environment, it can either slow down or speed up tumor growth. [1][4][5] IL-10 has strong anti-inflammatory properties that help reduce chronic inflammation. Chronic inflammation is a major risk factor for cancer. It can cause DNA damage, make the genetic material in cells unstable, and create a environment where tumors can form and grow. IL-10 is a special protein that helps control inflammation. It does this by reducing oxidative stress and inflammatory signals in the body. This helps to prevent tumors from forming.

DOI: 10.54254/2753-8818/96/2025.21969

High levels of IL-10 have been linked to better outcomes in some cancers, especially those where inflammation is a major cause. For example, in a type of liver cancer called hepatocellular carcinoma (HCC), IL-10 helps limit liver inflammation caused by chronic infections, such as hepatitis B and C, or conditions like non-alcoholic fatty liver disease. By reducing inflammation, IL-10 can prevent liver cell damage, fibrosis, and cancer.Additionally, IL-10 has been shown to directly inhibit the growth of certain tumor cells and promote the death of cancer cells, which contributes to its anti-tumor effects.

However, IL-10's role in cancer is not always beneficial. In many cases, IL-10 helps tumors grow and spread without being detected by the immune system. This happens because IL-10 can stop important immune cells that fight tumors from working. These cells include cytotoxic T lymphocytes (CTLs) and natural killer (NK) cells. High IL-10 levels in the tumor microenvironment can inhibit the production of interferon-gamma (IFN-γ), reduce antigen presentation by dendritic cells, and decrease the cytotoxic activity of CTLs and NK cells. This immunosuppressive environment enables cancer cells to evade immune surveillance, promoting tumor growth, invasion, and metastasis. [1,5] In cancers like melanoma, non-Hodgkin lymphoma, and certain solid tumors, high IL-10 levels are linked to a poor prognosis. IL-10 can help create regulatory T cells (Tregs) within the tumor. These Tregs can then suppress immune responses that fight the tumor. This immune suppression not only allows existing tumor cells to grow, but also reduces the effectiveness of immunotherapies, such as checkpoint inhibitors, which rely on active T cell responses to eliminate cancer cells. [1,5]

IL-10 has two different effects, which makes it hard to use as a treatment. In some cancers, increasing IL-10 might help reduce harmful inflammation and slow down tumor growth. In other cancers, decreasing IL-10 could help restore immune system activity and improve the body's ability to fight cancer. [1,6] For example, treatments that block IL-10 might be used to increase immunity against tumors in cancers where IL-10 helps the tumor hide from the immune system. On the other hand, treatments using a form of IL-10 that is made in a lab are being studied for cancers where inflammation is a key part of the disease.

In summary, IL-10's role in cancer depends on a fine balance between its ability to reduce inflammation and its ability to suppress the immune system. It is very important to understand the specific type of cancer, the tumor environment, and the patient's immune status to decide whether IL-10 should be used to activate or inhibit it in cancer therapy. [1,6]

4.1. IL-10 and Cancer Treatment

Understanding IL-10's multifaceted role has opened new avenues for cancer therapy. [4,6] IL-10's dual nature, acting as both an anti-inflammatory agent and an immunosuppressive factor, makes it a promising yet complex target for cancer treatment. Therapeutic strategies aim to either enhance or inhibit IL-10 signaling, depending on the specific cancer type and the desired immune response. For cancers where IL-10 promotes tumor growth by suppressing the body’s natural immune defenses, therapies targeting IL-10 or its receptor (IL-10R) are being explored to boost anti-tumor immunity.[4,6] These therapies include IL-10 receptor antagonists, which block IL-10's interaction with immune cells, thereby restoring the activity of cytotoxic T lymphocytes (CTLs) and natural killer (NK) cells to recognize and destroy cancer cells.

Conversely, in cancers characterized by excessive inflammation, such as colorectal cancer or gastric cancer, increasing IL-10 activity can help suppress the inflammatory microenvironment, thereby reducing tumor progression. [4,6] Chronic inflammation in these cancers leads to DNA damage and promotes tumor growth. By enhancing IL-10 expression, it is possible to mitigate these inflammatory processes, reducing cancer cell proliferation and metastasis. Recombinant IL-10 therapy is being investigated for its potential to modulate inflammation while preserving essential immune functions.

DOI: 10.54254/2753-8818/96/2025.21969

Innovative approaches such as IL-10 gene therapy, monoclonal antibodies, and small-molecule inhibitors are currently under investigation. [6] IL-10 gene therapy involves delivering IL-10 genes directly into tumor tissues to regulate local immune responses. Monoclonal antibodies targeting IL-10 or IL-10R are designed to either block or stimulate IL-10 pathways, depending on the therapeutic goal. Small-molecule inhibitors are also being developed to modulate downstream signaling pathways activated by IL-10, providing more precise control over immune responses.

IL-10 also shows promise as a biomarker for predicting responses to immunotherapies, such as immune checkpoint inhibitors. [5,6] By monitoring IL-10 levels in patients, clinicians can assess how well an individual might respond to specific treatments. For example, high IL-10 expression may indicate a poor response to checkpoint inhibitors, as IL-10-mediated immune suppression could limit T-cell activation. Conversely, in some cases, IL-10 levels could predict a better response when combined with other immunomodulatory therapies.

Moreover, combining IL-10-based therapies with traditional cancer treatments like chemotherapy and radiation therapy may enhance therapeutic efficacy. [4,5] Chemotherapy and radiation often induce inflammation as a side effect, which can limit their effectiveness. IL-10 can potentially reduce these treatment-related inflammatory side effects, improving patient tolerance to therapy and enhancing overall treatment outcomes. [1] Additionally, IL-10's ability to modulate the immune environment may sensitize tumors to conventional therapies, increasing the likelihood of tumor regression.

4.2. Future Research Directions

Future research should focus on elucidating the context-specific roles of IL-10 in various cancer types and stages. [1,4] Since IL-10 can act as both a tumor suppressor and a promoter depending on the tumor microenvironment, understanding these dynamics is crucial. Investigating how IL-10 interacts with other cytokines, such as IL-6, IL-12, and TNF-α, as well as with immune checkpoints like PD-1/PD-L1 and CTLA-4, will provide a more comprehensive understanding of its functions.[5] These interactions may reveal new therapeutic targets for enhancing or inhibiting IL-10 signaling in specific cancer contexts.

Long-term clinical trials are essential to evaluate the safety and efficacy of IL-10-targeted therapies. [4,6] While preclinical studies and early-phase clinical trials have shown promising results, large-scale trials are needed to confirm these findings across diverse patient populations. These trials should also assess the potential side effects of IL-10 modulation, as altering immune responses can sometimes lead to unintended consequences, such as autoimmunity or immunodeficiency.

Additionally, exploring IL-10's role in combination with new treatments, such as immune checkpoint inhibitors, adoptive cell therapies (e.g., CAR-T cells), and cancer vaccines, may show that these treatments work better together. For instance, combining IL-10 inhibitors with checkpoint blockade therapies might help T-cells attack tumors that have developed ways to hide from the immune system. Similarly, enhancing IL-10 activity in conjunction with CAR-T cell therapies could help control inflammation and reduce the risk of cytokine release syndrome, a common side effect of these treatments.

5. Conclusion

Interleukin-10 (IL-10) plays a dual role in cancer biology, acting as both a protector against cancer and a facilitator of tumor growth, depending on the context. Its anti-inflammatory properties are vital for mitigating inflammation-related cancer risks, preventing DNA damage, and inhibiting tumor initiation. Chronic inflammation is a recognized contributor to cancer development, and IL-10's regulation of inflammatory responses is crucial for immune balance and tumor protection.

Conversely, IL-10 can enable cancer cells to evade immune detection, promoting tumor proliferation. Elevated IL-10 levels in certain cancers can inhibit immune cell-mediated cytotoxicity, presenting both challenges and opportunities for cancer research. To optimize treatment strategies, it is essential to comprehend the specific tumor microenvironment. IL-10 has therapeutic potential across various cancers, necessitating an understanding of the patient's cancer type and its microenvironment. In some cases, enhancing IL-10 may control disease progression by alleviating inflammation and tissue damage, while in others, inhibiting IL-10 could bolster immune responses against tumors. Researchers are advancing IL-10-based therapies, including gene therapy, monoclonal antibodies, and immunotherapy combinations, to enhance personalized cancer treatment. In summary, IL-10 embodies both challenges and opportunities in cancer research and treatment. Its intricate role necessitates a nuanced approach to therapeutic application, balancing the need to mitigate detrimental inflammation while preserving effective anti-tumor immunity. As research progresses, IL-10 may emerge as a pivotal component in cancer therapy, offering innovative treatment avenues and renewed hope for patients. Continued exploration of IL-10's clinical applications could enhance the effectiveness and personalization of cancer treatments.

References

[1] *Kubo M, Motomura Y. Transcriptional regulation of the anti-inflammatory cytokine IL-10 in acquired immune cells. Front Immunol. 2012;3:275. doi:10.3389/fimmu.2012.00275.*

[2] *Pils MC, et al. Monocytes/macrophages and/or neutrophils are the target of IL-10 in the LPS endotoxemia model. Eur J Immunol. 2010;40(2):443–448. doi:10.1002/eji.200939592.*

[3] *Wang MH, et al. Association of IL10 and other immune response- and obesity-related genes with prostate cancer. The Prostate. 2009;69(8):874–885. doi:10.1002/pros.20933.*

[4] *Zhang Y, et al. ESR1 regulates the obesity- and metabolism-differential gene MMAA to inhibit the occurrence and development of hepatocellular carcinoma. Front Oncol. 2022;12:899969. doi:10.3389/fonc.2022.899969.*

[5] *Li B, et al. Adipose tissue macrophages: implications for obesity-associated cancer. Military Med Res. 2023;10:1. doi:10.1186/s40779-022-00437-5.*

[6] *Oncotarget. The genetic correlation of IL-10 polymorphism with cancer risk. Oncotarget. 2017;8:100593-100602. doi:10.18632/oncotarget.10059*