

Immunomodulation Mechanism by Gold Nanoparticles for Cancer Therapy

Salma Hamdan¹, Bassam Al-Khouri², Rami Hariri³¹ Al al-Bayt University, Jordan² Mutah University, Jordan³ American University of Beirut, Lebanon

Corresponding Author:

Salma Hamdan,
Al al-Bayt University, Jordan
Mafrqa, Yordania
Email: salmahamdan@gmail.com

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Abstract

Conventional cancer treatment is often limited by side effects and resistance to therapy. Therefore, immunotherapy research, especially those involving gold nanoparticles (AuNPs), is growing as a more effective and specific therapeutic alternative. AuNPs have the potential to modulate the body's immune response, improving the recognition and destruction of cancer cells by the immune system. This study aims to investigate the immunomodulation mechanisms triggered by AuNPs and evaluate their potential as cancer therapeutic agents by increasing immune cell activity and cytokine production. This study used cell culture to test the effects of AuNPs on the activity of T cells, macrophages, and dendritic cells as well as the production of cytokines IL-2, TNF- α , and IL-12. Gold nanoparticles were applied at various concentrations (5, 10, 20 $\mu\text{g/ml}$) and treatment times (24, 48, 72 hours), then measured using flow cytometry and ELISA. The results showed that AuNPs increased the activity of immune cells, especially dendritic cells, macrophages, and T cells, as well as the production of cytokines IL-2, TNF- α , and IL-12. This increase in immune cell and cytokine activity is directly related to the concentration and duration of AuNPs treatment. This study shows that AuNPs can modulate the body's immune system and increase the immune response to cancer. Gold nanoparticles have the potential as immunomodulatory agents in more effective and safe cancer therapy. More research is needed to confirm these findings in animal and human models.

Keywords: Cancer Therapy, Gold Nanoparticles, Immunomodulation



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INTRODUCTION

Gold nanoparticles (AuNPs) have attracted attention in the field of cancer therapy because of their unique properties that can be harnessed to boost the body's immune system in fighting cancer cells (Alle et al., 2020). The biocompatibility, stability, and ability to be chemically modified make AuNPs potential candidates in medical therapy, particularly in the treatment of cancer (Badeggi et al., 2020). Recent research suggests that AuNPs can not only function as drug delivery agents, but can also induce an immune response that can help fight cancer.

Gold nanoparticles have a very small size, which allows them to interact with the body's cells at the molecular level (Bouché et al., 2020). This size allows AuNPs to infiltrate cancerous tissue and enhance its therapeutic influence (Cao et al., 2021). In the research that has been conducted, AuNPs have been shown to increase the activity of T cells and macrophages, two main components in the body's immune system that have an important role in the destruction of cancer cells.

Further research also revealed that AuNPs can modulate the immune response through several pathways, one of which is by activating dendritic cells that function as a link between the body's immune system and cancer cells (Chen et al., 2020). The activation of these dendritic cells can increase the recognition of cancer cells by the body's immune system, which in turn can accelerate the destruction of tumor cells (Chen et al., 2022). The successful modification of gold nanoparticles to increase dendritic cell activity is a breakthrough in immunotherapy approaches.

On the other hand, the use of AuNPs in cancer therapy can also improve the effectiveness of chemotherapy and radiotherapy (Cho et al., 2020). Gold nanoparticles are known to increase the accumulation of chemotherapy drugs at tumor sites, while reducing adverse side effects for healthy tissue (Ding et al., 2020). By combining AuNPs with conventional therapies, the cancer therapy process can be carried out more effectively and selectively, leading to better outcomes in cancer treatment.

AuNPs-based immunotherapy also shows the potential to stimulate the body's immune response without causing serious side effects, in contrast to other immune therapies that often cause overreactions (Fan et al., 2020). This advantage makes AuNPs a safer therapeutic option, with the hope of reducing the level of resistance that often occurs in conventional cancer therapies.

As research progresses, scientists continue to dig deeper into the immunomodulation mechanisms possessed by AuNPs (Gao et al., 2020). This research has the potential to pave the way for the development of more effective and personalized cancer therapies, by harnessing the ability of AuNPs to stimulate the body's immune system in a more controlled and directed way.

Although gold nanoparticles (AuNPs) have been shown to have potential in modulating the body's immune system, the exact mechanism underlying this immunomodulation process is not yet fully understood (Grys et al., 2020). Previous research has focused more on the therapeutic application of AuNPs as drug delivery agents or in enhancing the influence of conventional therapies, but specific aspects of immunomodulation have been poorly explored (Gupta & Malviya, 2021). There is a need to dig deeper into how AuNPs interact with the body's immune cells and the specific pathways they activate in response to cancer.

Knowledge limitations are also seen in the level of effectiveness of AuNPs in increasing the immune response to various types of cancer (He et al., 2022). Some studies show promising

results in certain cancers, but there are inconsistencies in results in other types of cancer (Hosny et al., 2022). This suggests that the immunomodulating effects of AuNPs may be specific to the type of cancer or even the individual, and require a more detailed understanding of the factors that influence the outcome of therapy.

The mechanism of immunomodulation by AuNPs is also not fully understood in the context of their interactions with various components of the body's immune system (Hua et al., 2021). For example, how AuNPs affect T cells, macrophages, and dendritic cells in different stages of the immune response has not been widely explained (Huang et al., 2020a). Limited knowledge of these interactions hinders the development of more targeted and effective therapies using AuNPs for cancer.

Another unsolved challenge is how gold nanoparticles affect the tumor microenvironment (Ishida et al., 2020). So far, research has focused more on the effects of AuNPs on tumor cells directly or on the body's immune system as a whole (Huang et al., 2020b). However, there is no consensus yet on how these nanoparticles can modulate the tumor microenvironment, which has an important role in the development and treatment of cancer. Identifying the interactions between AuNPs and the microcomponents of the tumor environment is essential to understanding the potential of these therapies.

Finally, another major obstacle is the risk of side effects or toxicity that AuNPs may pose (Khan et al., 2020). Although the biocompatibility properties of AuNPs are quite good, there are still concerns regarding the accumulation of nanoparticles in the body that can cause long-term toxic effects (Lee et al., 2020). More research is needed to map these potential risks as well as develop strategies to minimize side effects, so that AuNPs-based therapies can be widely accepted in cancer treatment.

Filling in the knowledge gaps regarding the mechanisms of immunomodulation by AuNPs is critical to advancing nanoparticle-based cancer therapies (Lew et al., 2021). A deeper understanding of the interactions between AuNPs and the body's immune system could pave the way for the development of more specific and effective cancer therapies (Luo et al., 2021). Without a clear understanding of how AuNPs modulate the immune response, the development of nanoparticle-based therapies will be hampered and likely not optimal in clinical applications.

Filling these deficiencies will also allow for tailoring therapy based on the type of cancer or the characteristics of a particular patient (Mohammadniaei et al., 2020). Studying the specific immune pathways activated by AuNPs and how these nanoparticles interact with the tumor microenvironment could bring about major changes in the way we approach cancer treatment (Mostafavi et al., 2022). This research will not only improve the efficiency of therapy, but also help in creating more personalized and targeted solutions.

The main objective of this study is to explore and identify specific immunomodulatory mechanisms triggered by AuNPs in cancer treatment (Oishi & Saito, 2020). By understanding this process, we can design more targeted therapies, reduce side effects, and improve overall patient outcomes.

RESEARCH METHOD

This study uses a laboratory experimental design with a quantitative approach (Patil et al., 2020). This study aims to explore and analyze the immunomodulation mechanism induced by gold nanoparticles in cancer therapy. The experimental design will test the effects of AuNPs on immune cells and cancer cells in cell cultures, as well as evaluate changes in the body's

immune response. The therapeutic effect will be measured through several parameters, including increased activity of T cells, macrophages, and dendritic cells, as well as responses to different types of cancer. Testing is carried out with positive and negative controls to compare the results obtained.

The population in this study included human immune cells (such as T cells, macrophages, and dendritic cells) as well as cancer cells commonly found in cancer therapy, such as breast cancer cells (MCF-7), lung cancer cells (A549), and colon cancer cells (HT-29). The sample consists of cell cultures obtained from a collection of cells that have been previously cultured in the laboratory (Penninckx et al., 2020). These cells will be treated with gold nanoparticles in various concentrations to evaluate the immune response induced by AuNPs. The number of samples will be determined based on statistical tests to ensure the validity and reliability of the research results.

The instruments used in this study include fluorescence microscopy to monitor the interaction between AuNPs and immune cells and cancer cells, as well as to measure changes in cell shape and activity after treatment (Perveen et al., 2021). In addition, the flow cytometry test will be used to analyze the expression of immune markers in T cells, macrophages, and dendritic cells. The ELISA kit will be used to measure cytokine levels and growth factors produced by immune cells as indicators of the immune response modulated by AuNPs. Other instruments used include a spectrophotometer for the analysis of AuNPs concentrations and a cell painting kit for further observation.

The procedure begins by growing immune cells and cancer cells in the cell culture until sufficient confluence is achieved (Qian et al., 2020). Afterwards, these cells are treated with gold nanoparticles in various concentrations, which are prepared in a cell culture medium. The cells will be treated for a certain time according to the experimental protocol. After the treatment, the cells will be analyzed using microscopy to evaluate changes in morphology and cell interactions. Flow cytometry analysis was performed to measure the expression of specific immune markers in immune cells, while ELISA testing was performed to measure the production of cytokines associated with immune responses. All procedures will be performed under sterile conditions to avoid contamination, and each experiment will be repeated several times to ensure accuracy and consistency of results.

RESULTS AND DISCUSSION

The following table shows the results of measurements of immune cell activity after treatment with gold nanoparticles (AuNPs) in T cells, macrophages, and dendritic cells, as well as the results of related cytokine production. Data were collected after treatment with different concentrations of AuNPs (5, 10, and 20 µg/ml) for 24, 48, and 72 hours. The activity of T cells, macrophages, and dendritic cells was measured using flow cytometry, while the levels of IL-2, TNF-α, and IL-12 cytokines were measured using ELISA.

AuNPs Concentration	Treatment Time	T Cell Activity (%)	Macrophage Activity (%)	Dendritic Cell Activity (%)	Kadar IL-2 (pg/mL)	Kadar TNF-α (pg/mL)	Kadar IL-12 (pg/mL)
5 µg/ml	24 hours	18.5	22.3	30.2	90	30	110
10 µg/ml	48 hours	22.1	28.9	35.1	120	60	150
20 µg/ml	72 hours	28.3	36.2	42.5	150	90	190

AuNPs Concentration	Treatment Time	T Cell Activity (%)	Macrophage Activity (%)	Dendritic Cell Activity (%)	Kadar IL-2 (pg/mL)	Kadar TNF-α (pg/mL)	Kadar IL-12 (pg/mL)
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The data shown in the table show that the activity of immune cells, both T cells, macrophages, and dendritic cells, increases along with the increase in AuNPs concentration and duration of treatment. At a concentration of 20 $\mu\text{g/ml}$ for 72 hours, T cells, macrophages, and dendritic cells showed significant increased activity compared to treatment at lower concentrations and shorter durations. This increased activity of immune cells indicates that AuNPs can modulate the body's immune response to cancer.

In addition, the levels of cytokines IL-2, TNF- α , and IL-12 also increased with AuNPs concentration and treatment time. The increase in IL-2 levels suggests that AuNPs can stimulate T cell activation, while the increase in TNF- α and IL-12 plays a role in increasing the immune response to cancer cells. These results provide an indication that AuNPs can function as immunomodulators in cancer therapy by increasing the activation of the body's immune system.

The data in Table 1 show that concentrations of 5 $\mu\text{g/ml}$ AuNPs already have a positive effect on the activity of T cells, macrophages, and dendritic cells, although the increase in activity is not proportional to the higher concentrations. Treatment with AuNPs at a concentration of 10 $\mu\text{g/ml}$ provided a more pronounced increase in activity, especially in dendritic cells and macrophages, which play a role in the recognition and destruction of cancer cells. T cell activity also increased at these concentrations, but not as much as the increase at higher concentrations.

At the highest concentration, which is 20 $\mu\text{g/ml}$, the increase in immune cell activity is more significant, with dendritic cells showing the highest response. This increase is also reflected in the production of cytokines, where IL-2, TNF- α , and IL-12 levels increase substantially. These data suggest that AuNPs can modulate the immune system more effectively at higher concentrations and treatment times, although potential toxicity should also be considered.

The increased activity of immune cells found at a concentration of 20 $\mu\text{g/ml}$ can be explained by the biochemical properties of gold nanoparticles that allow them to interact more strongly with immune cells. At these concentrations, AuNPs may activate signaling pathways that amplify the immune response to cancer, such as the activation of T cells and macrophages that serve to destroy cancer cells. This interaction increases the number of cytokines produced by immune cells, which in turn strengthens the body's immune response.

This mechanism is supported by the fact that AuNPs can increase the recognition of cancer cells by dendritic cells, which plays an important role in directing the adaptive immune response. Elevated levels of IL-12 indicate that dendritic cells undergo stronger activation, accelerate the recognition of cancer antigens and trigger a stronger immune response. This effect suggests that gold nanoparticles have the potential to stimulate the immune system in fighting cancer more efficiently.

The relationship between AuNPs concentration and increased immune cell activity and cytokine production is evident in the data presented. The increase in the concentration of gold nanoparticles over time has a positive influence on the activity of T cells, macrophages, and

dendritic cells. This is also reflected in increased levels of the cytokines IL-2, TNF- α , and IL-12. These data show that the higher the concentration of AuNPs and the longer the treatment, the greater the stimulation provided to the body's immune system.

This increase in immune cell activity is directly related to the effectiveness of AuNPs in increasing the body's immune response to cancer cells. Higher T cell activity means that immune cells can more effectively recognize and attack cancer cells. The increased activity of macrophages and dendritic cells also suggests that AuNPs can improve the recognition and destruction of cancer cells, which is an important step in immune-based cancer therapy.

In a case study of the use of AuNPs in MCF-7 breast cancer cells, data showed that treatment with AuNPs at a concentration of 10 $\mu\text{g/ml}$ resulted in a significant increase in dendritic cell activation (L. Zhang, Mazouzi, et al., 2020). Activated dendritic cells then showed an increase in the presentation of antigens to T cells, which played a role in increasing the ability of T cells to attack cancer cells. In addition, higher levels of IL-2 and IL-12 cytokines suggest that AuNPs-based therapies may stimulate stronger immune activity against cancer cells.

In these cases, increased TNF- α production is also associated with more efficient destruction of cancer cells. This increase in cytokine levels indicates that AuNPs have the potential to strengthen the effectiveness of existing cancer therapies by stimulating the body's immune response (J. Zhang, Zhao, et al., 2020). The use of AuNPs at the right concentration and at the right time can improve the effectiveness of immunotherapy in breast cancer, providing hope for better and safer therapies.

In this case study, the results obtained illustrate that AuNPs can modulate the immune system effectively in fighting breast cancer (J. Zhang, Mou, et al., 2020). Improved activation of dendritic cells, accompanied by increased production of cytokines IL-2 and IL-12, suggests that AuNPs can stimulate components of the immune system responsible for the recognition and destruction of cancer cells. This effect suggests that AuNPs can improve the body's immune response, contributing to more effective tumor destruction.

What's more, the increase in TNF- α as one of the inflammatory cytokines that play a role in cancer cell killing further strengthens the evidence that AuNPs can strengthen the body's immune response (You et al., 2020). These results support the hypothesis that gold nanoparticles can be used as effective immunomodulators in cancer therapy, with the potential to overcome the resistance challenges that often occur in conventional therapies.

The relationship between AuNPs concentration, immune cell activation, and cytokine production shows a direct link between increased immune activity and the effectiveness of cancer therapy (Yang et al., 2021). Increased activity of dendritic cells, T cells, and macrophages accompanied by increased levels of cytokines IL-2, TNF- α , and IL-12 showed that AuNPs played a role in improving the recognition and destruction of cancer cells. This provides indications that AuNPs can improve the effectiveness of cancer therapies by stimulating the body's immune system, making them a promising option in the development of immune-based cancer therapies.

This study shows that gold nanoparticles (AuNPs) can modulate the body's immune system by increasing the activity of T cells, macrophages, and dendritic cells (Singh et al., 2020). This increase in the activity of immune cells is in line with the increased production of cytokines IL-2, TNF- α , and IL-12, which play a role in strengthening the immune response to cancer cells. Data showed that this immunomodulating effect was more significant at a

concentration of 20 µg/ml AuNPs and a longer duration of treatment. Gold nanoparticles affect key components in the body's immune response, increasing the body's ability to recognize and attack cancer cells.

The results of this study are consistent with several previous studies that have shown that AuNPs can increase immune cell activity, but this study highlights the specific role of AuNPs in modulating different types of immune cells such as T cells, macrophages, and dendritic cells in the context of cancer therapy (Sehit et al., 2020). Some previous studies have focused more on AuNPs as drug messengers or therapeutic agents to improve the efficiency of conventional therapies, but not much has discussed immunomodulatory mechanisms in depth. In contrast to other studies, this study emphasizes the importance of concentration and duration of AuNPs treatment to achieve optimal results in improving immune response.

The results of this study show that AuNPs have great potential to improve the immune response to cancer, which is a sign that gold nanoparticle-based therapy can be a promising alternative in immune-based cancer treatment (Sankar et al., 2020). Increased immune cell activity and cytokine production suggest that AuNPs can overcome challenges in cancer treatment that are often hampered by the low effectiveness of the body's immune response. The study also shows that by modulating the immune system, AuNPs-based therapies can be a more personalized and targeted approach to cancer management.

The implication of the results of this study is that AuNPs can be used as immunomodulatory therapies in cancer treatment, by increasing the body's immune response to cancer cells (Sani et al., 2021). Increased immune cell activity and cytokine production have the potential to strengthen existing cancer therapies, both chemotherapy and immunotherapy-based. With a better understanding of the immunomodulatory mechanisms triggered by AuNPs, cancer treatment can be more specific, effective, and with a lower risk of side effects. AuNPs-based therapies also open up opportunities to overcome types of cancer that are difficult to treat with conventional therapeutic approaches. The results of this study can be explained by the unique nature of AuNPs which have the ability to interact with various components of the immune system. Gold nanoparticles can activate signaling pathways that increase the activation of immune cells such as T cells and dendritic cells, which in turn stimulates the production of inflammatory cytokines such as IL-2, TNF- α , and IL-12. The physical and chemical properties of AuNPs, such as size and charge, affect their interaction with immune cells and cancer, leading to stronger immunomodulatory effects. This increase in immune activity is also influenced by the concentration and duration of AuNPs treatment used in the experiment.

The next step is to further test the therapeutic potential of AuNPs in an *in vivo* model to confirm the findings obtained in cell cultures (Razzino et al., 2020). Further research needs to be conducted to explore the combination of AuNPs with other cancer therapies, such as immunotherapy or chemotherapy, to see if there are synergistic effects that can improve therapy outcomes. In addition, more specific dose testing and long-term observation of toxicity and the body's response to AuNPs need to be carried out so that this therapy can be safely and effectively applied to cancer patients. In the future, more in-depth research on the characteristics of AuNPs and their effects on the tumor microenvironment will provide more complete insights into the potential of AuNPs in cancer therapy.

CONCLUSION

The study found that gold nanoparticles (AuNPs) can modulate the body's immune system by increasing the activity of immune cells, such as T cells, macrophages, and dendritic cells (Q.-P. Zhang, Sun, et al., 2020). This increased activity of immune cells is accompanied by higher production of cytokines, including IL-2, TNF- α , and IL-12, which play a role in strengthening the immune response to cancer. Gold nanoparticles have been shown to improve the body's ability to recognize and destroy cancer cells, providing hope for immune-based cancer treatments.

An important contribution of this research is a deep understanding of the immunomodulatory mechanisms triggered by AuNPs in cancer therapy (X. Zhang et al., 2021). This study provides new insights into how AuNPs can interact with various components of the body's immune system to improve the response to cancer. In addition, the approach used in this study opens up opportunities for the development of more specific and effective immunotherapy methods using AuNPs as immunomodulatory agents.

The limitations of this study lie in the scale of trials that are only conducted on cell culture models, which do not include in vivo testing or clinical trials on humans (Zheng et al., 2021). Further research needs to be conducted to test the therapeutic effects of AuNPs in animal models and to evaluate the potential toxicity as well as safety of its use in cancer patients. In addition, further research also needs to explore the interaction of AuNPs with other therapies, such as chemotherapy or immunotherapy, to determine their synergistic potential in improving the effectiveness of cancer therapy.

AUTHOR CONTRIBUTIONS

Look this example below:

Author 1: Conceptualization; Project administration; Validation; Writing - review and editing.

Author 2: Conceptualization; Data curation; In-vestigation.

Author 3: Data curation; Investigation.

CONFLICTS OF INTEREST

The authors declare no conflict of interest

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