

Summary

Anticancer therapy encompasses a variety of strategies, among which chemoimmunotherapy – combining the effects of chemotherapy and immunotherapy – is gaining particular importance. Chemotherapeutic agents, in addition to their direct cytotoxic effects, can modulate the tumor microenvironment, increasing tumor cell immunogenicity and promoting activation of the immune response. Particularly promising is the use of modern drug delivery systems, such as nanoconjugates, in combination with cell-based therapy using modified dendritic cells and cytokine modulation. Cytokines such as IL-12, IL-15, and IL-18 play a key role by influencing, among other things, the activation of NK cells and CD8⁺ T lymphocytes, while dendritic cells initiate a specific antitumor response.

Such an integrated approach enables a synergistic effect, leading to more effective inhibition of tumor growth and induction of a long-lasting antitumor response. As a result, chemoimmunotherapy is considered one of the most promising directions in the development of experimental oncology.

The aim of the research presented in this dissertation was to obtain genetically modified bone marrow-derived dendritic cells (BMDCs) capable of overproducing IL-12, IL-15, or IL-18, and to determine the role of these BMDCs in the activation and polarization of the antitumor response in chemoimmunotherapy of murine MC38 colon carcinoma and murine B16 melanoma.

The doctoral dissertation consists of a series of four thematically related publications: one review article and three original research papers.

The first publication, from 2019, entitled “Perspectives for the application of interleukin 15 in anti-cancer therapy” is a literature review focusing on the biological properties of IL-15 and its potential clinical applications. The paper emphasizes that IL-15 can stimulate the proliferation and activation of NK cells and CD8⁺ T lymphocytes, support the formation of immunological memory, and act synergistically with other immunotherapies. It also discusses limitations of IL-15 therapy, such as its short biological half-life and the possibility of side effects, highlighting the need for further research into optimal administration regimens. This review provided an important theoretical foundation for subsequent experimental studies.

The original research paper from 2023, entitled “The modulation of local and systemic anti-tumor immune response induced by methotrexate nanoconjugate in murine MC38 colon carcinoma and B16 F0 melanoma tumor models” presents experimental results on the effects of a methotrexate nanoconjugate (HES-MTX) on the immune response in murine models of

MC38 colon carcinoma and B16 melanoma. The findings, including the phenotype of tumor-infiltrating cells and analysis of systemic immune responses, enabled the selection of an immunomodulatory dose of the chemotherapeutic agent and the design of a therapeutic regimen for subsequent chemoimmunotherapy experiments.

The third paper, entitled “Inhibition of MC38 colon cancer growth by multicomponent chemoimmunotherapy with anti-IL-10R antibodies, HES-MTX nanoconjugate, depends on application of IL-12, IL-15 or IL-18 secreting dendritic cell vaccines” was also published in 2023. It compares the effectiveness of immunotherapy based on modified dendritic cells and anti-IL-10R antibodies with chemoimmunotherapy, in which the HES-MTX nanoconjugate was administered once prior to immunotherapy. The use of the HES-MTX nanoconjugate created a favorable environment for the effective action of cell-based vaccines, which was particularly evident in groups receiving dendritic cell-based vaccines as mixtures of two or three transductants. This publication provided a direct basis for further research on the application of combination therapy in other tumor models.

The fourth and most recent paper, published in 2026, entitled “Co-delivery of IL-12/IL-15/IL-18 engineered DC vaccines with anti-IL-10R and nanoconjugated methotrexate in melanoma” evaluates the effectiveness of a similar therapeutic strategy in a murine B16 melanoma model. The developed approaches led to inhibition of tumor growth, with the rate of tumor progression depending on the type of dendritic cell-based vaccine used. It was also demonstrated that, in this tumor model, the beneficial effect of nanoconjugate administration was mainly due to a reduction in the population of suppressor-type cells. This work constitutes a significant extension of previous studies, highlighting differences between immune responses in colon cancer and melanoma models, as well as emphasizing the translational potential of the developed chemoimmunotherapy strategy combining cytokine modulation, cell therapy, and nanoconjugated chemotherapeutics.

The presented publications form a coherent research pathway – from a theoretical review of the role of IL-15 to advanced strategies of multicomponent chemoimmunotherapy – providing a solid foundation for further experimental and translational applications in anticancer therapy.