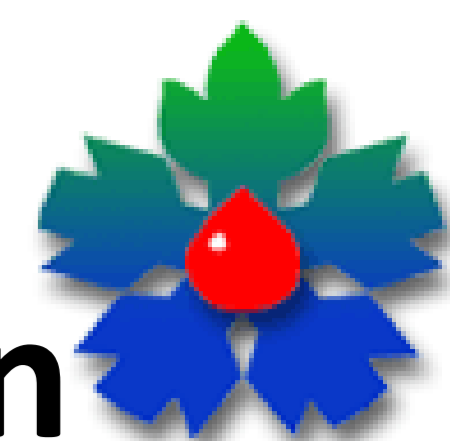


# Effect of nano-complexes based on vanadium nanoparticles and cholesterol on immune system of tumor-bearing animals



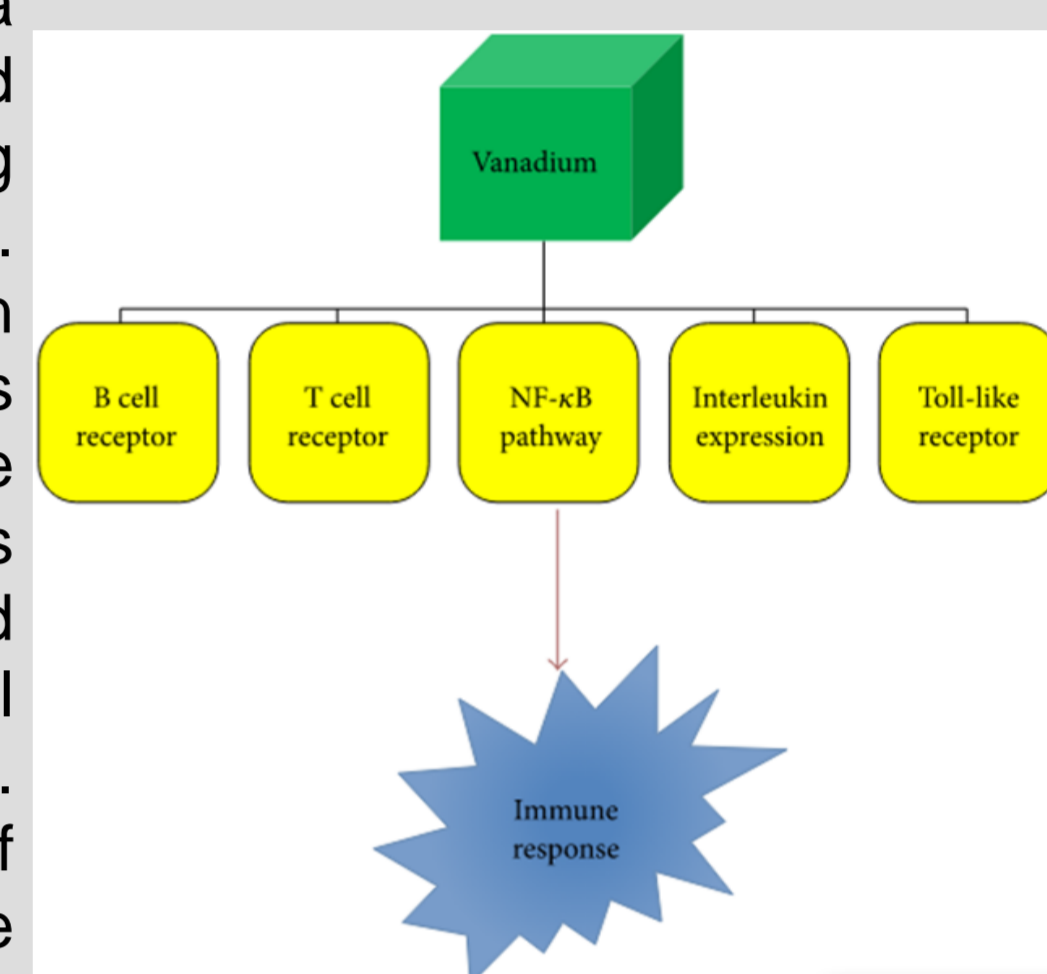
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Vanadium-based nanomaterials exhibit several types of biological activity and have the potential to be used as a pharmaceutical drug. Vanadium can exist as a free ion in one of three states; vanadium (IV), vanadium (V), and the most stable form in aqueous solutions - vanadium (III). Each ion is able to bind to different proteins, forming metalloprotein complexes that differ in stoichiometry, charge, structure, and reactivity in the biological system [1]. The involvement of vanadium ions in the mechanisms of immunoregulation, including the support or suppression of the inflammatory reaction, is known, which makes it necessary to study the effect of various forms of vanadates on the body for the purpose of effective immunotherapy. This opposite effect may be a consequence of the interaction of nanoparticles (NPs) with components of both innate and acquired immunity. The interaction of cells of the immune system with the tumor is a delicate balance between the processes of immune activation and immunosuppression. There are works that show the role of vanadium compounds in the regulation of T-cell signaling, which allows them to be considered as promising antitumor drugs with an immunomodulatory effect. The interaction of cells of the immune system with the tumor is a delicate balance between the processes of immune activation and immunosuppression. There are works that show the role of vanadium compounds in the regulation of T-cell signaling, which allows them to be considered as promising antitumor drugs with an immunomodulatory effect.



The purpose of the study was to evaluate the effect of nanocomplexes (NCs) containing rare-earth orthovanadates GdYVO<sub>4</sub>:Eu<sup>3+</sup> and cholesterol on the growth of Ehrlich ascites carcinoma (EAC) and changes in the immune system indices of tumor-bearing recipients.

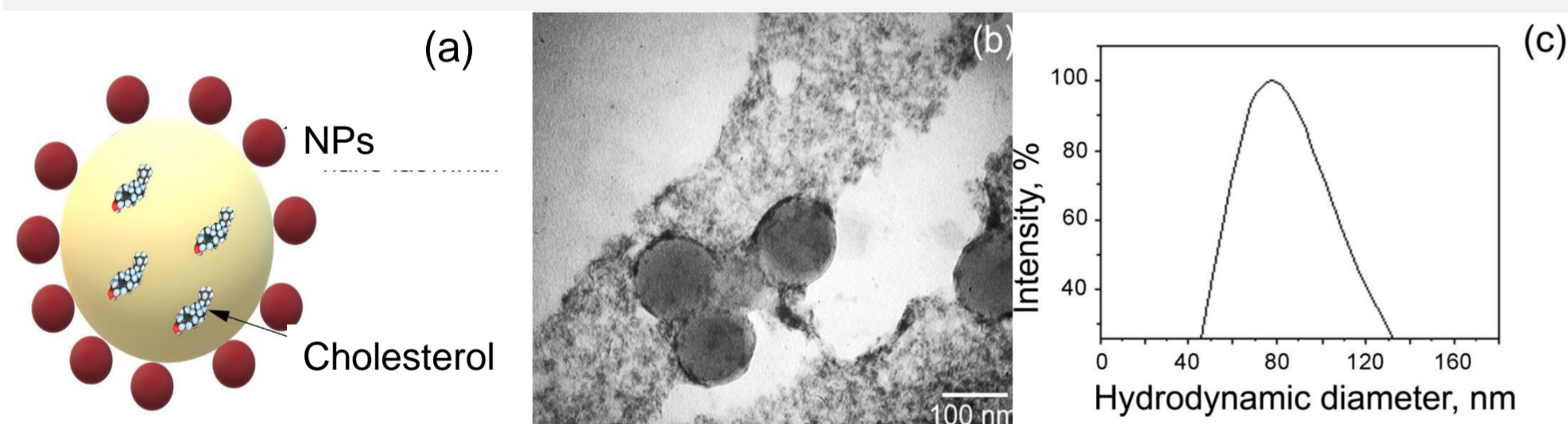
## Materials and methods

### Nanocomplex:

(a) Schematic representation

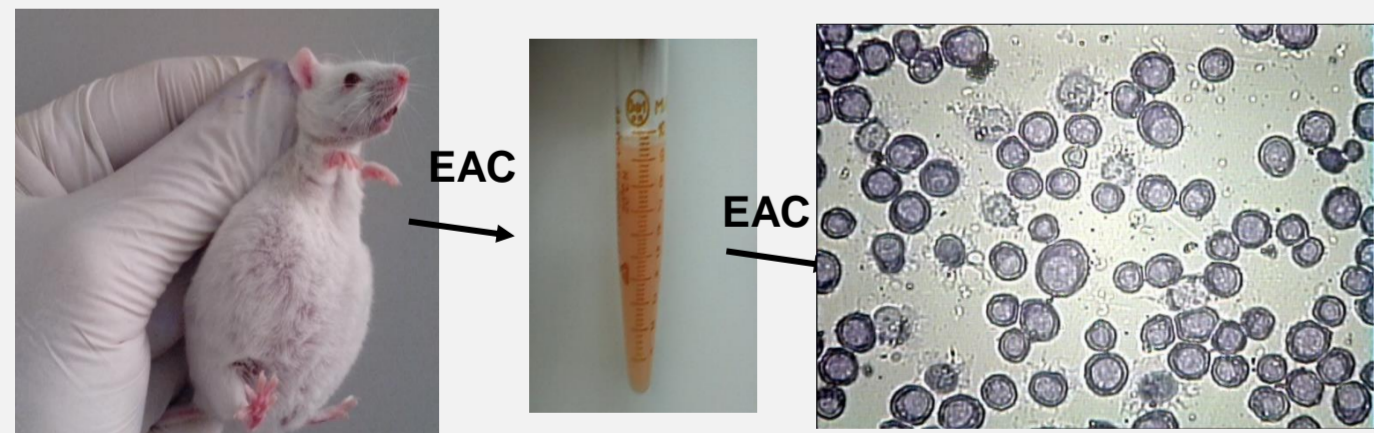
(b) transmission electron microscopy photomicrography

(c) measurement of the hydrodynamic diameter



The nanocomplex, synthesized first at the Institute for Scintillation Materials of the National Academy of Sciences of Ukraine, is the product of aqueous dispersion of cholesterol (0,55 g/l) and NPs (1.3 g/l) of rare earth orthovanadates (GdYVO<sub>4</sub>:Eu<sup>3+</sup>) composition [2].

### Cells of the ascitic form of EAC, which is a cell line of undifferentiated breast cancer cells



Incubation *in vitro* at room temperature for 3 h  
900 µl of cells +  
100 µl of NCs

### Three groups of mice were formed:

1. Animals injected with native EAC cells (n=10).
2. Animals injected with EAC cells + NCs (n=10).
3. Intact animals - control (n=10).

### Assessment of EAC cells parameters on the 4th, 7th and 14th days of *in vivo* cultivation:

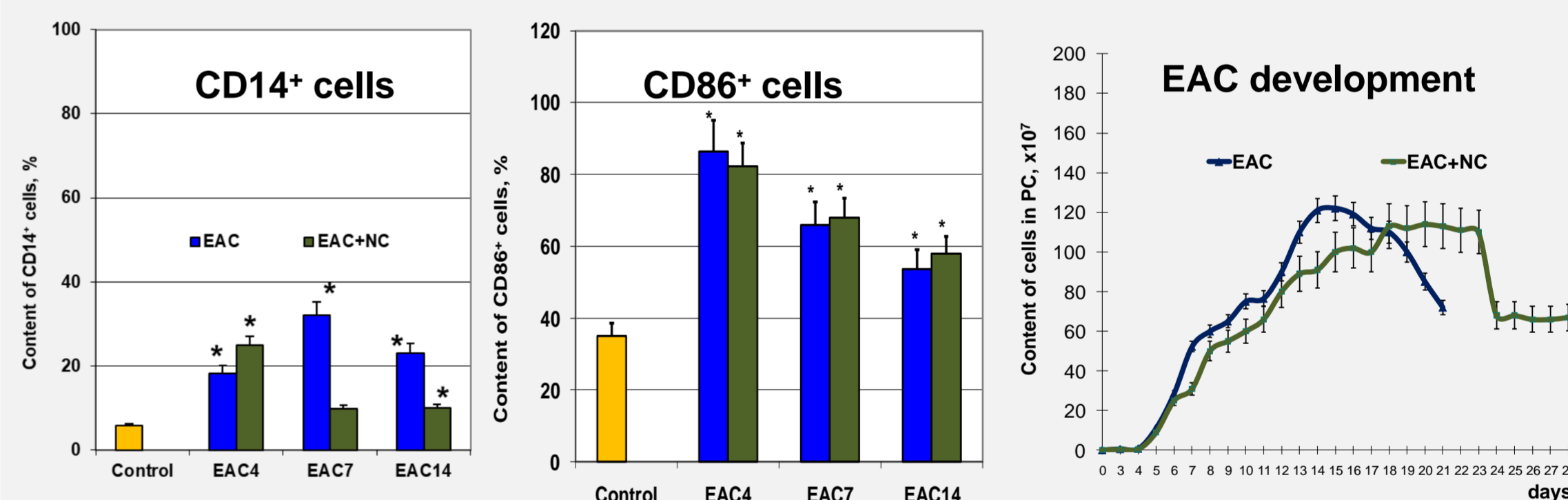
-the absolute number of cells and the content of CD14<sup>+</sup>, CD86<sup>+</sup> cells in the peritoneal cavity

-phenotypic markers of immunocompetent cells in inguinal lymph nodes (CD4<sup>+</sup>, CD8<sup>+</sup>, CD16/32<sup>+</sup>, CD4<sup>+</sup>CD25<sup>+</sup>)

-animal survival

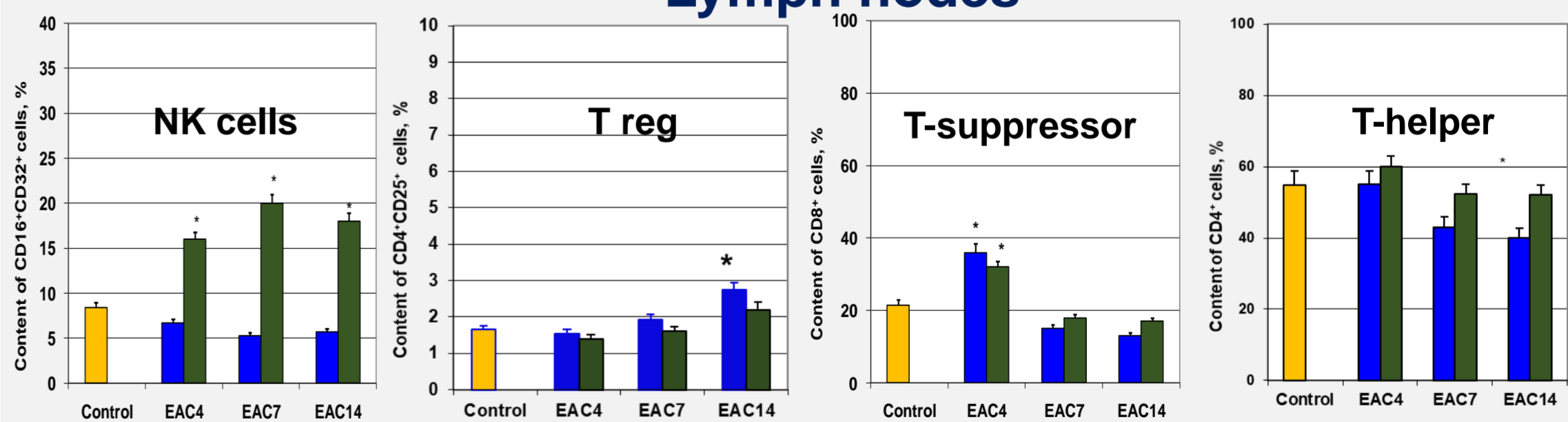
## Results

### Peritoneal Cavity

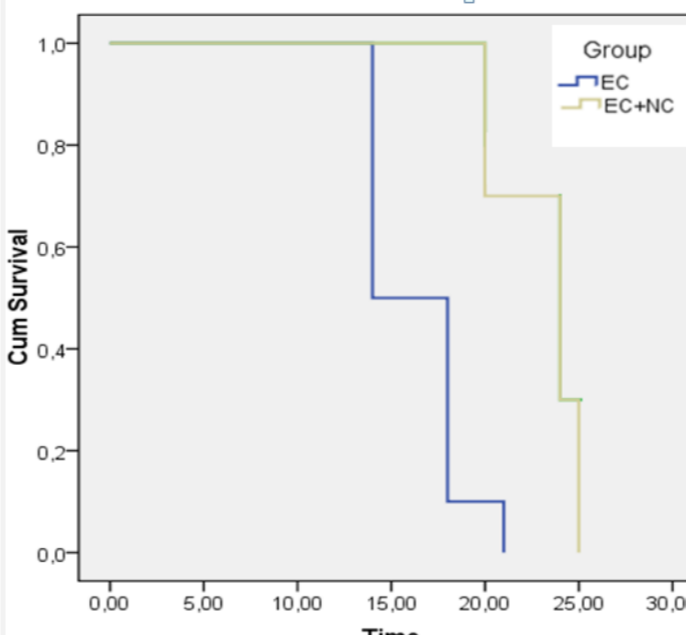


Induction of EAC by cells pretreated with NCs led to the activation of mononuclear phagocytic system (MPS) cells in the peritoneal cavity. This contributed to reducing the intensity of tumor growth and prolonging the lifespan of tumor-bearing animals.

### Lymph nodes



### Survival mice



It was established that the development of EAC, the number of all subpopulations of immunocompetent lymph node cells that were determined gradually decreased, with the exception of the subpopulation of T-regulatory (CD4<sup>+</sup>CD25<sup>+</sup>) cells. This indicates the gradual development of the immunosuppressive state of the tumor-bearing animals, which created favorable conditions for the development of EAC. Induction of oncological pathology by tumor cells pre-treated with NCs resulted in the inhibition of tumor growth by 74.70±4.38%. This was accompanied by an increase in the number of natural killer cells (CD16/32<sup>+</sup>) and a decrease in the content of T-regulatory cells.

## Conclusions

The use of NCs leads to the inhibition of the growth inhibition of EAC cells in mice and mediates the activation of the antitumor activity of the immune system of tumor-bearing animals due to a decrease in the number of regulatory T cells and an increase in the number of natural killer cells. The results obtained can be taken into account when creating new strategies for cancer therapy.

[1] Tsave O., Petanidis S., Kioseoglou E., et al. Role of Vanadium in Cellular and Molecular Immunology: Association with Immune-Related Inflammation and Pharmacotoxicology Mechanisms. Oxid Med Cell Longev. 2016;2016:4013639.

[2] Klochkov VK (2015) Method for producing water dispersion of cholesterol. Patent of Ukraine 108011