EFFECT OF E.COLI PHAGE LYSATE VACCINATIONS ON CD4+ CD25+ FOXP3+ T-REGULATORY CELLS AND CYTOKINE LEVELS IN CANCER BEARING MICE

K. Gambashidze1, I. Pantsulaia2, M. Iobadze2, A. Azaladze1, K. Kalandarishvili3, P. Khorava4, E. Jaiani5, B. Lasareishvili5
1Pathophysiology, Tbilisi State Medical University, Tbilisi, GEORGIJA
2Immunology, Tbilisi State Medical University, Tbilisi, GEORGIA
3Clinical Anatomy, Tbilisi State Medical University, Tbilisi, GEORGIA
4Surgery, Georgian National Cancer Center, Tbilisi, GEORGIJA
5Phages, Eliava Institute of Bacteriophage, Microbiology and Virology, Tbilisi, GEORGIA

Aim: Regulatory T cells (Treg) play a key role in maintaining the balance of immune responses in human health and in disease. Generally, Tregs are considered as the most powerful inhibitors of antitumor immunity and the greatest barrier to successful immunotherapy and vaccinations. Modulation of Tregs can enhance the efficacy of cancer immunotherapy and has potential to result in tumor regression. The aim of this study was to stimulate antitumor innate immunity via suppression of Treg and activation of effector immune cells using E.coli phage lysate vaccinations.

Methods: Specimen (spleen, blood serum) were obtained from control (with Ehrlich carcinoma) and E.coli phage lysate vaccinated (0.25 ml/day, with 5 day intervals, during 5 weeks) 20–25 g C57BL/6J mice. Number of CD4+CD25+FoxP3+ Treg as well as CD3+CD4+, CD3+CD8+, NK1.1 cells were assessed using FACS Array Bioanalyzer (BD FACSCalibur, USA) and WST-8 Cell Proliferation Assay Kit. Isolated cells were stained by fluorochrome conjugated antibodies (anti-CD3, Foxp3), NK1.1, anti-CD4, anti-CD8, anti-CD25 and isotype-matched controls). Two-color data analysis for CD4CD8, CD3CD4, CD4CD25, CD25Foxp3 staining was performed using dot plots with WinMDI Software. Cytokines: IL-12, TGF-β, IFN-γ were studied by ELISA according to manufactures protocol (R&D systems; BD Biosciences).

Results: Investigations have shown that E.coli phage lysate vaccinations stimulate innate and further acquired immunity manifested by increase in NK1.1, CD3CD4, CD3CD8 cells and secretion of IL-12, IFN-γ with further decrease in TGF-β, CD4CD25, CD25Foxp3 compared to control. More than 5 vaccinations had no effect and further vaccinations decreased immune response. Our results indicate that although vaccinations enhance antitumor immunity and host defenses decreasing Tregs and stimulating CD3+CD4+, CD3+CD8+, NK1.1 effector immune cells, the successful treatment requires optimal regimen of vaccination.

Conclusions: E.coli phage lysate vaccinations have in vivo antitumor immunomodulatory effect and can be considered as a new immunotherapeutic approach of cancers.

Disclosure: All authors have declared no conflicts of interest.