

12th Euro Biotechnology Congress

November 07-09, 2016 Alicante, Spain

The development of a novel drug on the basis of conjugates of cytokines with bisphosphonates for the treatment of bone metastases

Elena Dmitriyevna Danilenko, G M Sysoyeva, E I Ryabchikova, A I Zakabunin, E A Volosnikova, G M Levagina and S G Gamaley
Federal Budgetary Research Institution State Research Center of Virology and Biotechnology "Vector", Russia

The interest to tumor necrosis factor alpha (TNF α) and interferon gamma (IFN γ) as drug agents for the treatment of bone metastases is explained by antitumor properties of these proteins as well as by their ability to regulate the remodeling processes in bone tissue. Bisphosphonates characterized by the ability to accumulate in bone tissue and to regulate the activity of osteoclasts/osteoblasts can be used as vector molecules for the targeted delivery of cytokines into the bone. The purpose of this study was to develop the method for synthesizing the conjugates of TNF α and IFN γ with bisphosphonate alendronic acid (ALN) and to explore their antitumor activity. The conjugates of TNF α or IFN γ with ALN were obtained by the synthesis on a solid media using 1-ethyl-3-[3-dimethylaminopropyl] carbodiimide hydrochloride. The method involving the fixation of active components on a solid phase yielded conjugates of high degree homogeneity (up to 95.7%) and a stoichiometry close to 1:1. The output of conjugates in the synthesis reaction was 90 \pm 3%. In an experimental model of bone metastases of melanoma B16-F10, induced in C57Bl/6 mice by intracardiac administration was showed that the conjugates of TNF α -ALN and IFN γ -ALN had the ability to trigger necrotic changes in the tumor tissue, covering 40-90% and 30-100% of the metastasis area, respectively. The administration of TNF α -ALN conjugates reduced melanoma lesions of epiphyseal and diaphyseal bone tissue of the femur. These findings confirm the prospects of further development of a novel drug based on the conjugates of cytokines for the treatment of bone metastases.

Biography

Elena Dmitriyevna Danilenko was graduated from Novosibirsk State University and defended her dissertation for PhD in 2006. She is currently the Director of the Institute of Medical Biotechnology, the branch of the State Research Center of Virology and Biotechnology "Vector". She is the author of more than 50 articles in refereed journals and 4 patents.

danilenko_ed@vector.nsc.ru

Notes: