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The immune system contributes to the treatment with nanotherapeutics

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N-(2-hydroxypropyl) methacrylamide (HPMA)-based copolymers containing doxorubicin or taxanes exert *in vivo* dual cytostatic and immunostimulating activity. The treatment regularly triggers systemic specific anticancer resistance that protects mice from a second cancer attack. Such therapy-inducible auto vaccination is dose and time dependent. More aggressive treatment which facilitates very rapid elimination of antigen/tumor cells induces low or even undetectable tumor resistance, whereas a slow eradication of tumor mass induces a strong tumor resistance. As proven by neutralization Winn's test, the chief mediators of the phenomenon are $CD8^+$ cytotoxic T lymphocytes (CTL) and memory cells. Mice suffering from acute tumor model responded to the therapy much better if compared with mice suffering from chronic tumor model. Such treatment-triggered cancer resistance could be explained by immunoprotective character of macromolecular therapeutics and their ability to induce immunogenic cancer cell death. We have detected in mouse EL4 T cell lymphoma exposed to DOX-HPMA translocation of calreticulin, ERp57 and HSPs (60, 70, 90, and 110) and release of high-mobility-group box 1 protein (HMGB1). Moreover, *in vitro* treatment of EL4 and mouse B cell lymphoma 38C13 increases phagocytosis by dendritic cells while engulfment of similarly treated normal cell is not enhanced due to high expression of CD47. Mice treated with "immunosafe" polymeric conjugates showed significantly lower cancer cell infiltration in inguinal (ipsilateral) lymph nodes if compared to mice treated with free doxorubicin.

Biography

Rihova Blanka is Professor of Immunology, Charles University, Prague, Czech Republic and Adjunct Professor of Pharmaceutics and Pharmaceutical Chemistry, University of Utah, Salt Lake City, Utah, USA. In 2000-2007, she was the Director of the Institute of Microbiology, Academy of Sciences of the Czech Republic. She is a member of Scientific Councils of the Academy of Sciences of the Czech Republic and of the Charles University and an elected member of Czech Learned Society, European Academy of Sciences and European Academy of Sciences and Arts. She is the President of the Czech Immunological Society.

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