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Professor Kateryna Bielka
Medical Research Archives Senior Editor

Dear Professor Bielka,

I am sending the manuscript entitled,
"**Potentiation of cancer immunity-inducing effect by pH-sensitive polysaccharide-modified liposomes with combination of TGF-β type I receptor inhibitor-embedded liposomes**", which I would like to publish in Medical Research Archives.

The importance of immunotherapy is increasing for efficient cancer therapy. Therefore, many efforts have been made to develop antigen delivery systems for effective induction of cancer-specific immunity using liposomes, polymeric micelles, nanogels and virus-based systems. Among them liposomes are advantageous from the practical viewpoint because of excellent biodegradability and safety. Therefore, liposome-based antigen delivery systems have been intensively studied.

We have developed liposomes modified with pH-sensitive poly(glycidol) derivatives or pH-sensitive dextran derivatives which are destabilized in endosome and enhance the transfer of the content into cytoplasm [E. Yuba et al., **Biomaterials**, **31**, 943-951 (2010), E. Yuba et al., **J. Control. Release**, **149**, 72-80 (2011), & E. Yuba et al., **Biomaterials**, **35**, 3091-3101 (2014)] and showed that these liposomes are promising as antigen delivery systems. In fact, these pH-sensitive polymer-modified liposomes delivered antigenic protein OVA into cytosol of dendritic cells (DCs) and induced antigen-specific cellular immunity and therapeutic effects on tumor-bearing mice [E. Yuba et al., **Biomaterials**, **34**, 3042-3052 (2013), E. Yuba et al., **Biomaterials**, **34**, 5711-5721 (2013), & E. Yuba et al., **Biomaterials**, **35**, 3091-3101

(2014)]. In addition, the combination of immune-activating functions (adjuvant functions) with pH-sensitive polymer-modified liposomes further increased their immunity-inducing effects [Y. Yoshizaki et al., **Biomaterials**, **35**, 8186-8196 (2014), E. Yuba et al., **Biomaterials**, **67**, 214-224 (2015), & E. Yuba et al., **Biomaterials**, **120**, 32-45 (2017)].

Based on the previous studies, in this study, we developed a new type of liposome-based immunity-inducing system using both pH-sensitive dextran derivative-modified liposomes and TGF-β signaling inhibitor-embedded liposomes. TGF-β signaling induces immunosuppressive responses in microenvironment of tumor, which leads the progression of tumor by escaping from cancer-specific immunity. TGF-β signaling inhibitor-embedded liposomes canceled immunosuppressive effects in mice and simultaneously cancer-specific cellular immunity was induced by pH-sensitive dextran derivative-modified liposomes, resulting in stronger therapeutic effects on tumor-bearing mice than those of our previous systems (**Biomaterials**, **34**, 3042-3052 (2013), **Biomaterials**, **35**, 8186-8196 (2014)).

We believe that this study is of importance for the creation of potent vaccine systems which lead to establishment of safe and effective cancer immunotherapy. Therefore, the paper should provide valuable information to researchers engaged in the field of immunotherapy and related bioactive molecule-based therapies and their delivery technologies.

Thank you very much for your help.

Sincerely yours,

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