Liposomal formulation of polyacrylate-peptide conjugate as a new vaccine candidate against cervical cancer

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Submitted: October 3, 2018
Accepted: October 25, 2018

From the Clinical Editor:

The number of women affected by cervical cancer worldwide is very significant and the disease is associated with human papilloma virus (HPV) infection. Although the use of HPV vaccines has proven to be useful in disease protection, they only work in women who have never been infected by HPV previously. Thus, the development of a therapeutic vaccine that targets HPV-infected cells is needed for women who are already infected with the virus. In this study, the authors describe the use of a self-adjuvating polymer-based delivery system for the development of a therapeutic vaccine. Therefore, while efforts are progressing, vaccine candidates are still required against late stage cervical cancer via improving the vaccine delivery system. Authors demonstrate that the combination of polymer-based and liposome delivery systems may be effective without the use of additional adjuvant and with just a single dose immunization. This finding has potential importance for other cancer vaccines as well.

Abstract

Peptide-based vaccines have been proposed as a therapeutic strategy for many infectious diseases, including human papilloma virus (HPV)-related cervical cancer. Peptide-based vaccines are a better treatment option than traditional chemotherapeutic agents and surgery, as they rely on the use of the body’s immune system to fight cancer cells, resulting in minimal risk of side effects. However, to increase the efficacy of peptide-based vaccines, the application of potent adjuvant and a suitable delivery system is essential. In this study, we developed a self-adjuvating delivery system based on a combination of polymer and liposomes, for a therapeutic vaccine against cervical cancer. Peptide epitope (8Qm) derived from HPV-16 E7 protein was conjugated to dendritic poly(tert-butyl acrylate) as a primary delivery system and incorporated into cationic liposomes, which served as a secondary delivery system. Our vaccine candidate was able to kill established HPV-16 E7-positive tumor (TC-1) cells in mice following a single immunization. The immunized mice had 80% survival rate after two months. In contrast, both polymer-8Qm conjugate and liposomes bearing 8Qm failed to eradicate TC-1...
tumors. The survival rate of mice was only 20% when immunized with 8Qm formulated with standard incomplete Freund’s adjuvant.

RESEARCH ARTICLES

Prec. Nanomed. 2018 Oct;1(3):173-182

Nanoparticle-Encapsulated Doxorubicin Demonstrates Superior Tumor Cell Kill in Triple Negative Breast Cancer Subtypes Intrinsically Resistant to Doxorubicin

Krausz AE, Adler BL, Makdisi J, Schairer D, Rosen J, Landriscina A, Navati M, Alfieri A, Friedman JM, Nosanchuk JD, Rodriguez-Gabin A, Ye KQ, McDaid HM, Friedman AJ.

Submitted: July 18, 2018

From the Clinical Editor:

POTENTIAL CLINICAL SIGNIFICANCE

The treatment of triple-negative breast cancer is often difficult due to frequent resistance to doxorubicin. Using different nano-formulations based on sol-gel technology to encapsulate doxorubicin, the authors here showed enhanced dose-response metrics and tumor cell kill of these cancer cells due to an increased drug accumulation in the local tumor environment. This platform shows early promise in terms of eventual clinical translatability.

Abstract

The effect of size and release kinetics of doxorubicin-nanoparticles on anti-tumor efficacy was evaluated in a panel of human cancer cell lines, including triple-negative breast cancer (TNBC) cells that frequently demonstrate resistance to doxorubicin. Different nano-formulations of sol-gel-based Doxorubicin containing nanoparticles were synthesized. Increased cell kill in chemorefractory triple-negative breast cancer cells was associated with the smallest size of nanoparticles and the slowest release of Dox. Modeling of dose-response parameters in Dox-sensitive versus Dox-resistant lines demonstrated increased EMax and area under the curve in Dox-resistant mesenchymal TNBC cells, implying potentially favorable activity in this molecular subtype of breast cancer. Mesenchymal TNBC cells demonstrated a high rate of fluorescent bead uptake suggestive of increased endocytosis, which may partially account for the enhanced efficacy of Dox-np in this subtype. Thus, manipulation of size and release kinetics of this nanoparticle platform is associated with enhanced dose-response metrics and tumor cell kill in therapeutically recalcitrant TNBC cell models. This platform is easily customizable and warrants further exploration.

Prec. Nanomed. 2018 Oct;1(3):194-207.

Specific Molecular Recognition as a Strategy to Delineate Tumor Margin Using Topically Applied Fluorescence Embedded Nanoparticles

Barton S, Li B, Siuta M, Janve VA, Song J, Holt CM, Tomono T, Ukawa M, Kamagai H, Tobita E, Wilson K, Sakuma S, Pham W.

Submitted: October 9, 2018

From the Clinical Editor:

BASIC RESEARCH

Surgical resection remains the main treatment modality for pancreatic cancer. Thus, the ability to delineate the tumor accurately during operation is important to ensure all tumor cells are resected. Here, the authors describe the development of a multimodal imaging probe using nanospheres to target epithelial cells of pancreatic cancer. The specificity to target only tumor cells was clearly shown in both in-vitro and in-vivo experiments. This technology may provide a new fluorescence imaging technique to help the field of surgical oncology in the future.

ABSTRACT

The Thomsen-Friedenreich (TF) antigen is a tumor-associated antigen consistently expressed on the apical surface of epithelial-based cancer cells, including pancreatic cancer. In this work, we report the development of a multimodal imaging probe, the tripolymer fluorescent nanospheres, whose surface was fabricated with peanut agglutinin (PNA) moieties as TF molecular recognition molecules. Here, we demonstrate that the probe is able to detect TF antigen in human pancreatic cancer tissues and differentiate from normal tissue. What is most noteworthy regarding the probe is its ability to visualize tumor margins defined by epithelial TF antigen expression. Further, in vivo preclinical studies using an orthotopic mouse model of pancreatic cancer suggest the potential use of the nanospheres for laparoscopic imaging of pancreatic cancer tumor margins to enhance surgical resection and improve clinical outcomes.
Plasma samples from mouse strains and humans demonstrate different in vitro susceptibilities to complement activation

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Submitted: October 29, 2018
Accepted: November 21, 2018

From the Clinical Editor:

Preclinical characterization of nanotechnology-based products is essential for translating innovative applications into clinics. In addition to the innate immune system complement activation plays an important role in regulating the adaptive immune response. Undesirable activation of the complement system in response to new composites may lead to hypersensitivity reactions. The authors describe the importance of mouse strain selection for in vitro complement activation analysis addressing also the existence of inter- and intraspecies variability.

Abstract

Complement activation can be evaluated in vitro using plasma or serum from animals and human donors, and in vivo using animal models. Despite many years of research, there is no harmonized approach for the selection of matrix and animal models. Herein, we present an in vitro study investigating intra- and inter-species variability in the complement activation. We used the liposomal formulation of amphotericin, AmBisome, as a model particle to assess the magnitude of the complement activation in plasma derived from various mouse strains and individual human donors. We demonstrate that mouse strains differ in the magnitude of complement activation by liposomes and cobra venom factor in vitro. Inter-individual variability in complement activation by AmBisome and cobra venom factor was also observed when plasma from individual human donors was analyzed. Such variability in both mouse and human plasma could not be explained by the levels of complement regulatory factors H and I. Moreover, even though mouse plasma was less sensitive to the complement activation by CVF than human plasma, it was equally sensitive to the activation by AmBisome. Our study demonstrates the importance of mouse strain selection for in vitro complement activation analysis. It also shows that traditional positive controls, such as cobra venom factor, are not predictive of the degree of complement activation by nanomedicines. The study also suggests that besides complement inhibitory factors, other elements contribute to the inter- and intra-species variability in complement activation by nanomedicines.