Bacterial Membrane Nanoparticles as an Immunotherapy System for Cancer Treatment

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WARF: P180331US02

The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in developing improved cancer immunotherapy treatments. UW–Madison researchers have engineered a novel nanoparticle that elicits an improved immune response in select melanomas for significant tumor suppression.

OVERVIEW

Cancer immunotherapy – a therapy that stimulates and employs the body’s own immune system – is one of the most promising new approaches for treating cancer. Despite its tremendous potential, it shows limited effectiveness on patients with immunogenically “cold” tumors, as these tumors remain “hidden” from immune cells. Radiation therapy has been shown to improve the immunotherapy by turning a “cold” tumor into a “hot” one, thereby highlighting tumor cells for immune cell recognition. Significant effort has gone into stimulating immune cells to recognize tumor cells, but available methods are limited and often result in modest therapeutic benefit.

THE INVENTION

UW–Madison researchers have engineered a bacterial membrane-coated nanoparticle (BNP) capable of acting as a cancer treatment/vaccine. The BNP consists of a nanosized polyplex made up of a PC7A polymer, a CpG oligonucleotide inside the bacterial membrane and surface attached maleimide (Mal) groups. PC7A provides both a pH responsiveness, which allows for membrane interactions at neutral pH, and subsequent endosomal escape once internalized into the cell. CpG functions as an immunostimulatory molecule (as a toll-like receptor agonist). And Mal groups decorate the surface of the BNP to capture tumor remnants created by radiation treatment, accelerating cellular recognition of the tumor.

In combination with radiation therapy, the inventors show that BNP treatment led to significant tumor growth suppression and enhanced survival rate in a model of a B78 melanoma tumor, a hard cancer to treat. By enabling patients’ immune systems to recognize the unique antigens on their own tumors, this combination therapy may represent a universal approach to achieve personalized cancer immunotherapy using off-the-shelf agents.

THE WARF ADVANTAGE

WARF: A Leader in Technology Transfer Since 1925
Since its founding as a private, nonprofit affiliate of the University of Wisconsin–Madison, WARF has provided patent and licensing services to UW–Madison and worked with commercial partners to transform university research into products that benefit society. WARF intellectual property managers and licensing staff members are leaders in the field of university-based technology transfer. They are familiar with the intricacies of patenting, have worked with researchers in relevant disciplines, understand industries and markets, and have negotiated innovative licensing strategies to meet the individual needs of business clients.

The University of Wisconsin and WARF – A Single Location to Accelerate Translational Development of New Drugs
UW–Madison has the integrative capabilities to complete many key components of the drug development cycle, from discovery through clinical trials. As one of the top research universities in the world, and one of the two best-funded universities for research in the country, UW–Madison offers state-of-the-art facilities unmatched by most public universities.

These include the Small Molecule Screening Facility at the UW Comprehensive Cancer Center; the Zeep Pharmaceutical Experiment Station, which provides consulting and laboratory services for developing formulations and studying solubility, stability and more; the Waisman Clinical Biomanufacturing Facility; the Wisconsin Institute for Medical Research, which provides UW–Madison with a complete translational research facility; and the innovative, interdisciplinary Wisconsin Institutes for Discovery, home to the private, nonprofit Morgridge Institute for Research and its public twin, WID, part of the university’s graduate school. The highly qualified experts at these facilities are ready to work with you to create a library of candidates for drug development.
APPLICATIONS

• Improved recognition of host immunity during cancer immunotherapy

KEY BENEFITS

• In combination with radiation, BNP suppresses tumor growth and improves survival rate in B78 melanoma mouse model.
• BNP has no observable systemic toxicity.
• BNP production is easier and more cost-effective than similar nanoparticle approaches.

ADDITIONAL INFORMATION

Publications

Tech Fields
Pharmaceuticals & Vitamin D - Oncology & hematology

CONTACT INFORMATION

For current licensing status, please contact Rafael Diaz at rdiaz@warf.org or 608-960-9847.

FIGURES

Figure 1. Schematic of the in situ vaccine effect elicited by combined RT + BNP. A) A schematic of how a BNP interacts with the TME to enhance APC uptake and activation. B) Schematic depiction of the in situ vaccine effect elicited by combined RT + BNP. After RT stimulates neocarcinogen release, BNP is intramuscularly injected to capture antigens. The BNP-neocarcinogen complex then undergoes highly efficient APC uptake and immune response due to the TLR9 agonists present on the BNP’s bacterial membrane coating. Once the BNP is endocytosed, CpG is released from the polypeptide core and activates TLR9, which is located at the inner membrane of the endosomes, thereby prompting APC maturation. PCTA, another component of the polypeptide, facilitates the endosomal escape of neocarcinogens via membrane disruption. The neocarcinogens in CpG are degraded into small peptides by proteases and presented by MHC complexes. Finally, the mature APCs present neocarcinogens to CD4+ and CD8+ T cells and secrete cytokines that activate cancer immunity. C) Composition of the BNP and the function of each BNP component.