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Virus-Like Nanoparticles for Non-Capsid Antigen Delivery with Virus Structure/Functional Mimicry to Activate B Cell Immunity

Project Number
1R01AI154072-01

Contact PI/Project Leader
SUN, DUXIN Other PIs

Awardee Organization
UNIVERSITY OF MICHIGAN AT ANN ARBOR

Description

Abstract Text

Various nanoparticles (NPs) have been used for delivery of small antigens, which have limited viral mimic features and are more efficacious than soluble antigens in stimulating B-cell immunity. However, these traditional NPs lack characteristics of virus “spiky capsid protein peplomer”, e.g. spiky antigen clusters on the peplomers, optimal distance between antigen clusters, and highly localized antigen density on the spike. It is unknown how the lack of virus-like features of traditional NPs affect B cell immunity and durable antibody responses. Although virus-like features of B cell vaccine for durable B cell immunity are clinically validated using virus-like particles (VLPs) of viral capsid proteins, VLPs are not suitable for delivery of non-capsid small antigens (such as bacterial toxins, small molecules, and oncogenic peptides) since these non-capsid small antigens are not able to self-assemble to VLPs. There is a need to develop virus-like nanoparticles for small antigens to activate B cell immunity against deadly bacterial toxins (**Anthrax**, Botulinum), small molecules, and oncogenic peptides. Three components of B cell immunity are critical for durable antibody response: (A) Efficient antigen delivery/retention and unique antigen distribution patterns for B cell acquisition in the draining lymph nodes (dLNs), (B) Activation of antigen-specific B cells through multivalent binding/crosslink with B cell receptor (BCR), (C) Activation of follicular T Helper cells (Tfh) that support Germinal Center (GC) B cells and their differentiation to long-lived plasma cells (LLPCs). However, it is unknown how the lack of virus-like features of NPs antigen delivery systems affect these three critical components of B cell immunity for durable antibody response. In this proposal, we will generate inorganic virus like nanoparticles (IVLNs) with three features of spiky peplomers of virus' using four types of small antigens (peptides of **anthrax** and botulinum toxins, small molecule 4-hydroxy- 3-nitrophenyl acetyl-hapten, HER2 peptides) to test our hypothesis. We hypothesize that: (A) Virus-like features of IVLNs enhance efficient delivery/retention with unique antigen distribution patterns for B cell acquisition in the lymph node, (B) Virus-like features of IVLNs enhance B cell activation via multivalent bind/crosslink with B cell receptor, promote follicular T (Tfh) cell-dependent B-cell activation, enhance formation of long-lived plasma cells (LLPCs) in the Germinal Center (GC), and generate antibodies with high specificity/affinity, (C) Virus-like features of IVLNs induce durable antibody response against bacterial toxins (**anthrax** and botulinum) and oncogenic antigens. Aim 1 Determine virus-like features of IVLNs to improve antigen delivery/retention with unique antigen distribution patterns for B cell acquisition in the lymph nodes vs. traditional NPs Aim 2 Identify the stages of B cell responses by the virus-like features of IVLNs vs. traditional NPs Aim 3 Investigate IVLNs-antigen immunizations to induce more durable antibody response against **Anthrax** and Botulinum toxins and oncogenic HER2 in animals vs. traditional NPs

Public Health Relevance Statement

We expect to engineer inorganic virus-like nanoparticles (IVLNs) for delivery of non-capsid small antigens, which not only mimic the structural features of virus peplomer, but also exhibit virus-like function in induction of antigen- specific B cells and durable antibody responses. The IVLNs have broad applications to activate B cell immunity against non-capsid small antigens, such as bacterial toxin to prevent/treat bacterial infection (anthrax or botulinum), oncogenic antigen in prevention/treatment of cancers, and high affinity/specificity antibody production against small molecules and small peptides.

NIH Spending Category

Anthrax Bioengineering Biotechnology Emerging Infectious Diseases Infectious Diseases Nanotechnology Prevention Rare Diseases

Project Terms

Affect Affinity Animals **Anthrax** disease Antibodies Antibody Formation Antibody Response Antibody Specificity Antibody titer measurement Antigens B-Cell Activation B-Lymphocytes Bacterial Infections Bacterial Toxins Binding Botulinum Toxins Capsid Proteins Clinical Development ERBB2 gene Engineering Exhibits Haptens Helper-Inducer T-Lymphocyte Immunity Immunization Malignant Neoplasms Memory B-Lymphocyte Oncogenic Pattern Peptides Plasma Cells Prevention Receptors, Antigen, B-Cell Specificity Structure Structure of germinal center of lymph node Supporting Cell System T-Lymphocyte Testing Vaccines Viral Virus Virus-like particle

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Awardee Organization
UNIVERSITY OF MICHIGAN AT ANN ARBOR

ASSOCIATE PROFESSOR

Contact
duxins@umich.edu

clapham@mail.nih.gov

Organization

Name
UNIVERSITY OF MICHIGAN AT ANN ARBOR

City
ANN ARBOR

Country
UNITED STATES (US)

Department Type
PHARMACOLOGY

Organization Type
SCHOOLS OF PHARMACY

State Code
MI

Congressional District
12

Other Information

FOA
PA-19-056

Study Section
Gene and Drug Delivery Systems Study Section[GDD]

Fiscal Year
2020

Award Notice Date
07-July-2020

Administering Institutes or Centers
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

DUNS Number
073133571

CFDA Code
855

Project Start Date
07-July-2020

Project End Date
30-June-2025

Budget Start Date
07-July-2020

Budget End Date
30-June-2021

Project Funding Information for 2020

Total Funding
$513,210

Direct Costs
$328,981

Indirect Costs
$184,229

Year	Funding IC	FY Total Cost by IC
2020	NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	$513,210

NIH Categorical Spending

Click here for more information on NIH Categorical Spending

Funding IC	FY Total Cost by IC	NIH Spending Category
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	$513,210	Anthrax; Bioengineering; Biotechnology; Emerging Infectious Diseases; Infectious Diseases; Nanotechnology; Prevention; Rare Diseases;

Sub Projects

No Sub Projects information available for 1R01AI154072-01

Publications

No Publications available for 1R01AI154072-01

Patents

No Patents information available for 1R01AI154072-01

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Clinical Studies

No Clinical Studies information available for 1R01AI154072-01

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Related News Releases

No news release information available for 1R01AI154072-01

History

No Historical information available for 1R01AI154072-01

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