Back to Search Results

Description
Details
Sub-Projects
Publications
Patents
Outcomes
Clinical Studies
News and More
History
Similar Projects

Immunity to novel T/F SHIVs: variability in the co-evolution of virus and host immunity

Project Number	Contact PI/Project Leader	Awardee Organization
5R01AI128832-03	KELSOE, GARNETT H	DUKE UNIVERSITY

Description

Abstract Text

Statement of Work The HIV-1 **pandemic** is a global threat and effective vaccination is the most likely pathway to its control. While vaccines that induce broadly neutralizing antibodies (bNAbs) against HIV could be transformative for intervening in the HIV **pandemic**, no vaccine has been shown to induce HIV-1 bNAbs. Indeed, we do not even understand how bNAb responses arise in rare, HIV-1 infected patients. In part our failure to understand HIV-1 immunity and the generation of bNAb responses can be traced to the absence of a suitable experimental model to study virus:host interaction. Most simian-human immunodeficiency viruses (SHIVs) bearing envelope (Env) glycoproteins from primary HIV-1 strains do not infect rhesus macaques (RMs). This failure reflects low affinity for rhesus CD4 (rhCD4) resulting in impaired virus entry into rhCD4+ cells. We have solved the issue of Env-rhCD4 binding and demonstrated productive infection in RMs by SHIVs with T/F Env glycoproteins, including those that elicit broadly neutralizing antibodies (bnAbs) in humans. The goal of this study is to study infection and immunity in rhesus macaques infected with molecular clones of T/F SHIVs to determine whether patterns of co-evolution by virus and host immunity in individual macaques are similar or unique. This issue is crucial in predicting the efficacy of “lineage design” vaccines.

Public Health Relevance Statement

Relevance HIV-1 infection and AIDS is a global threat not only to the health of individuals but to societies and nations. It is clear that vaccines capable of eliciting broadly neutralizing HIV-1 antibody (bNAb) could be highly effective in stemming the HIV pandemic, at present no vaccine has been shown to induce HIV-1 bNAbs. A widely used approach to induce bnAb production by vaccination is the development of “designer” immunogens that recreate known pathways of bnAb evolution. This approach, however is always based on the bnAb response of rare individuals. The experiments proposed in this application will determine whether immune response to identical T/F viruses are similar between individual RMs or highly distinct. This is a crucial point for “lineage design” vaccines: if immune responses are highly variable to identical infections, then the recapitulation of any single bnAb lineage in diverse individuals is unlikely.

NIH Spending Category

Biotechnology HIV/AIDS Immunization Infectious Diseases Prevention Vaccine Related Vaccine Related (AIDS)

Project Terms

Acquired Immunodeficiency Syndrome Affinity Age Anecdotes Antibodies Antibody Formation Antibody Response Antigens Autologous B-Lymphocytes Binding Cell Lineage Cells Clone Cells Cloning Data Correlations Development Dose Evolution Experimental Models Failure Generations Genetic study Glycoproteins Goals HIV HIV-1 Health Human Humoral Immunities Immune Immune response Immunity Impairment Individual Infection Knowledge Laboratories Macaca Macaca mulatta Maps Memory Methods Molecular Molecular Cloning Natural History Nature Pathway interactions Patients Pattern Plasma Population Problem Solving Production Reproducibility Route Serologic tests Societies

Read More

Details

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Back to Search Results

Description
Details
Sub-Projects
Publications
Patents
Outcomes
Clinical Studies
News and More
History
Similar Projects

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Project Number
5R01AI128832-03

Contact PI/Project Leader
KELSOE, GARNETT H

Awardee Organization
DUKE UNIVERSITY

Country
UNITED STATES (US)

Other Information

FOA
RFA-AI-15-055

Study Section
Special Emphasis Panel[ZRG1-AARR-P(51)R]

Fiscal Year
2019

Award Notice Date
11-July-2019

Administering Institutes or Centers
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

DUNS Number
044387793

CFDA Code
855

Project Start Date
01-July-2017

Project End Date
30-June-2022

Budget Start Date
01-July-2019

Budget End Date
30-June-2020

Project Funding Information for 2019

Total Funding
$1,303,208

Direct Costs
$969,910

Indirect Costs
$333,298

Year	Funding IC	FY Total Cost by IC
2019	NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	$1,303,208

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	$1,303,208	Biotechnology; HIV/AIDS; Immunization; Infectious Diseases; Prevention; Vaccine Related; Vaccine Related (AIDS);

Sub Projects

No Sub Projects information available for 5R01AI128832-03

Publications

No Publications available for 5R01AI128832-03

Patents

No Patents information available for 5R01AI128832-03

Outcomes

The Project Outcomes shown here are displayed verbatim as submitted by the Principal Investigator (PI) for this award. Any opinions, findings, and conclusions or recommendations expressed are those of the PI and do not necessarily reflect the views of the National Institutes of Health. NIH has not endorsed the content below.

No Outcomes available for 5R01AI128832-03

Clinical Studies

No Clinical Studies information available for 5R01AI128832-03

Back to Search Results

Description
Details
Sub-Projects
Publications
Patents
Outcomes
Clinical Studies
News and More
History
Similar Projects

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No news release information available for 5R01AI128832-03

History

No Historical information available for 5R01AI128832-03

Similar Projects

No Similar Projects information available for 5R01AI128832-03