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Role of female genital mucosa associated CD4 T cells in vaccine-induced HIV susceptibility

Project Number
1R21AI143454-01

Contact PI/Project Leader
IYER, SWAMINATHAN SMITA

Awardee Organization
UNIVERSITY OF CALIFORNIA AT DAVIS

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Description

Abstract Text

Project Summary Vaccine-triggered CD4 T cell help is essential for establishing long-lived humoral and cellular immunity and is central to HIV vaccine efficacy. But, CD4 is also the major receptor for HIV which raises concerns as to whether vaccine induced CD4 T cells could subvert vaccine efficacy; a premise supported by the STEP trial and several HIV vaccine studies in non-human primates, including our own. The cellular mechanisms underlying the paradox of vaccine-induced susceptibility to HIV remain poorly articulated, and yet identifying the mechanism involved is the first step to effective vaccine design. This proposal is focused on understanding CD4 T cells in the female genital tract (FGT), the major portal of HIV entry by heterosexual transmission. In Aim 1 of this research project, we will investigate functional characteristics of highly vulnerable HIV target CD4 T cells within the genital tract of HIV uninfected humans and rhesus macaques. In Aim 2 of this proposal, we will investigate how a DNA-prime/protein boost vaccination regimen, a widely used HIV vaccine platform, impacts the phenotype of FGT associated HIV target CD4 T cells. We will determine whether vaccine-specific CD4 T cells in the FGT express key markers of HIV vulnerability and whether this is driven by vaccine induced changes in the cytokine milieu. We will also determine how preventing migration of vaccine-induced cells to the FGT impacts the vaginal inflammatory environment. Finally, we will elucidate dynamics of vaccine-induced CD4 T cells in the FGT after simian (S)IV exposure and explore cells disseminated to the rectal mucosa and lymphoid tissue. The chances of ameliorating the virus is greatest in the earliest stages of infection, at the mucosal point of entry; thus, our findings could lay the foundation for determining whether inhibiting the migration of HIV target cells to the FGT during the post-vaccination effector phase is a strategy to decrease vaccine-induced susceptibility to HIV.

Public Health Relevance Statement

Project Narrative The majority of HIV infections by heterosexual transmission occur in women; understanding factors contributing to this increased risk is critical to prevent HIV infection in women and curb the global HIV/AIDS pandemic. This proposal uses robust complementary approaches and cutting-edge immunological tools to address this concern. Accomplishment of proposed goals will aid in designing interventions in women to prevent HIV infection.

NIH Spending Category

Biotechnology | Clinical Research | HIV/AIDS | Immunization | Infectious Diseases | Prevention | Vaccine Related | Vaccine Related (AIDS) | Women's Health

Project Terms

AIDS/HIV problem | Address | Animal Model | Binding | Biopsy | CCR5 gene | CD4 Positive T Lymphocytes | Cell Cycle Progression | Cells | Cellular Immunity | Cervical | Characteristics | DNA | Data | Environment | Female | Foundations | Gene Expression Profile | Generations | Genes | Genital system | Goals | Gut associated lymphoid tissue | HIV | HIV Infections | HIV Receptors | HIV Seronegativity | HIV vaccine | HIV/SIV vaccine | Heterosexuals | Human | Humoral Immunities | Immune | Immunity | Immunobiology | Immunologics | Infection | Inflammation | Inflammatory | Integrins | Intestines | Knowledge | Lymphoid Tissue | Macaca | Macaca mulatta | Mediating | Modeling | Molecular | Mucositis | Mucous Membrane

Read More

Details

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Awardee Organization
UNIVERSITY OF CALIFORNIA AT DAVIS

City
DAVIS

Country
UNITED STATES (US)

SCHOOLS OF MEDICINE

03

Other Information

FOA
PA-18-489

Study Section
HIV/AIDS Vaccines Study Section[VACC]

Fiscal Year
2019

Award Notice Date
04-December-2018

Administering Institutes or Centers
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

DUNS Number
047120084

CFDA Code
855

Project Start Date
05-December-2018

Project End Date
30-November-2020

Budget Start Date
05-December-2018

Budget End Date
30-November-2019

Project Funding Information for 2019

Total Funding
$235,500

Direct Costs
$150,000

Indirect Costs
$85,500

Year	Funding IC	FY Total Cost by IC
2019	NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	$235,500

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	$235,500	Biotechnology; Clinical Research; HIV/AIDS; Immunization; Infectious Diseases; Prevention; Vaccine Related; Women's Health;
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	$117,750	Vaccine Related (AIDS)

Sub Projects

No Sub Projects information available for 1R21AI143454-01

Publications

No Publications available for 1R21AI143454-01

Patents

No Patents information available for 1R21AI143454-01

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 1R21AI143454-01

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News and More

Related News Releases

No news release information available for 1R21AI143454-01

History

No Historical information available for 1R21AI143454-01

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No Similar Projects information available for 1R21AI143454-01