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Pathogenesis of Uveitis in Ebola Virus Disease Survivors

Project Number Contact PI/Project Leader 1R01EY029594-01A1 YEH, STEVEN

Awardee Organization EMORY UNIVERSITY

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Abstract Text

Project Summary/ Abstract Ebola virus disease (EVD) has been associated with a high prevalence of uveitis in EVD survivors in the wake of the unprecedented West African EVD outbreak from 2014-2016. The spectrum of disease ranges from anterior uveitis to sight-threatening panuveitis with complete blindness. The sheer number of EVD survivors impacted has given us the unique opportunity to characterize the clinical features, structural complications leading to vision loss, and pathogenesis of uveitis. Besides the significant impact of vision loss on quality-of-life and activities of daily living, uveitis associated with Ebola virus (EBOV) has scientific and public health implications because of our prior identification of EBOV in the aqueous humor. Beyond the recent outbreak in West Africa, two more recent outbreaks in Democratic Republic of Congo underscore the global health mandate to fully understand the clinical and scientific implications of EVD sequelae. Emerging clinical, basic, and translational investigation has provided insight regarding the potential mechanisms of uveitis associated with EVD. We recently described our novel methodology to safely interrogate aqueous humor specimens for EBOV in EVD survivors; while these ocular fluid specimens tested negative for EBOV by RT-PCR, recent molecular pathologic analysis of ocular tissue in a non-human primate EVD survivor model has demonstrated that EBOV persists within the vitreous humor in macrophages, and is associated with uveitis and retinitis. Additional compelling immunologic studies of an EVD survivor with uveitis showed Ebola-specific T-cell and B-cell activation with signs of ongoing Ebola antigen stimulation after plasma clearance of EBOV. These findings were suggestive of long-term EBOV persistence, which are detectable by systemic T- and B-cell responses. To further characterize the prevalence and clinical spectrum of uveitis, role of EBOV persistence and immunologic mechanisms of uveitis in EVD survivors, we propose three Aims: 1) In Aim 1, the prevalence of uveitis will be compared between EVD survivors and close contacts in Sierra Leone. Clinical factors and host risk factors including HLAtyping will be assessed to determine if there are clinical and host-related determinants of uveitis development. 2) In Aim 2, EBOV persistence will be assessed using reverse transcriptase polymerase chain reaction (RT- PCR testing) of vitreous fluid and in situ hybridization techniques to detect EBOV genome in the vitreous. 3) In Aim 3, Ebola-specific immune responses will be assessed in the blood and ocular fluid of EVD survivors with uveitis, specifically evaluating activation of Ebola-specific B and T-cells, IgG subclass composition. Insights from this study will define the spectrum of uveitis associated with EVD, assess whether EBOV is harbored in the vitreous, and advance our understanding of the interplay between infection and immunity in EVD. Ultimately, these findings will define diagnostic strategies and future medical countermeasures for EBOV, as well as other viruses that may establish persistence in the unique immune privileged ocular environment.

Public Health Relevance Statement

Project Narrative This study characterizes the pathogenesis of sight-threatening uveitis in Ebola virus disease (EVD) survivors, which has been associated with Ebola virus (EBOV) persistence in ocular fluid. We will assess the prevalence and clinical spectrum of uveitis, as well as host-disease risk factors contributing to its manifestation. In addition, assessment of EBOV persistence in the vitreous and EBOV antigen-specific immune responses will impact our understanding of mechanisms of disease that will inform clinical care decision-making for EVD survivors and provide further insight into to other types of infectious uveitis.

NIH Spending Category

Biodefense Clinical Research Emerging Infectious Diseases Eye Disease and Disorders of Vision

Infectious Diseases Neurosciences Rare Diseases

Project Terms

Activities of Daily Living Anterior uveitis Antibodies Acute Address **Africa** African **Aqueous Humor Antibody Response B-Cell Activation B-Lymphocytes Blindness Antigens Cessation of life** Blood Cells Clinical **Clinical Research Complete Blindness** Complication Country **Decision Making Democratic Republic of the Congo Diagnostic Detection Development Ebola Hemorrhagic Fever** Disease **Disease Outbreaks Ebola virus Epidemiology Environment Homing Evaluation Future Haplotypes High Prevalence** Household Eye Eye diseases Immune response **Immunity Immunologic Markers Immunologics Immune** Immunoglobulin G In Situ Hybridization Infection Inflammatory Investigation **Immunology** Laboratories

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Pathogenesis of Uveitis in Ebola Virus Disease Survivors

Contact PI/Project Leader Project Number Awardee Organization 1R01EY029594-01A1 YEH, STEVEN **EMORY UNIVERSITY**

Contact Title

mckiegeo@mail.nih.gov Contact

steven.yeh@unmc.edu

Organization

Name Department Type State Code

EMORY UNIVERSITY OPHTHALMOLOGY GA

Organization Type City **Congressional District SCHOOLS OF MEDICINE ATLANTA** 05

Country

UNITED STATES (US)

Other Information

Fiscal Year

FOA Administering Institutes or Centers 01-July-2019 Project Start

NATIONAL EYE INSTITUTE PA-18-484 Date

Study Section CFDA Code **DUNS Number** Special Emphasis Panel ZRG1

066469933 867 **BDCN-J (81)**

Award Notice Date

2019 20-June-2019 30-June-2020 **Budget End Date**

Project Funding Information for 2019

Total Funding Direct Costs Indirect Costs \$706,028 \$481,938 \$224,090

Funding IC Year **FY Total Cost by IC** 2019 NATIONAL EYE INSTITUTE \$706,028

NIH Categorical Spending

Click here for more information on NIH Categorical Spending

Project End Date

Budget Start

Date

30-June-2024

01-July-2019

Funding IC	FY Total Cost by IC	NIH Spending Category
NATIONAL EYE INSTITUTE	\$706,028	Biodefense; Clinical Research; Emerging Infectious Diseases; Eye Disease and Disorders of Vision; Infectious Diseases; Neurosciences; Rare Diseases;

品 Sub Projects

No Sub Projects information available for 1R01EY029594-01A1

Publications

No Publications available for 1R01EY029594-01A1

Patents

No Patents information available for 1R01EY029594-01A1

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.

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No Clinical Studies information available for 1R01EY029594-01A1

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Related News Releases

No news release information available for 1R01EY029594-01A1

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