SUMMARY STATEMENT
(Privileged Communication)

PROGRAM CONTACT: [redacted]

Release Date: **09/14/2018**

Revised Date:

Application Number: **1 K08 AI143391-01**

Principal Investigator

ANTAR, ANNUKKA AIDA ROSE

Applicant Organization: JOHNS HOPKINS UNIVERSITY

Review Group: **AIDS**
Acquired Immunodeficiency Syndrome Research Review Committee
AIDS - EXP. REV.

Meeting Date: **08/30/2018**
Council: **OCT 2018**
Requested Start: **12/01/2018**

RFA/PA: **PA18-373**
PCC: **A26K**

Project Title: **The HIV Latent Reservoir, Suboptimal Immune Response on Antiretroviral Therapy, and Exogenous Cytokine Therapies**
SRG Action: **Impact Score:** [redacted]
Next Steps: **Visit https://grants.nih.gov/grants/next_steps.htm**
Human Subjects: **10-No human subjects involved**
Animal Subjects: **10-No live vertebrate animals involved for competing appl.**

Project Year	Direct Costs Requested	Estimated Total Cost
1		
2		
3		
4		
5		
TOTAL	[redacted]	[redacted]

ADMINISTRATIVE BUDGET NOTE: The budget shown is the requested budget and has not been adjusted to reflect any recommendations made by reviewers. If an award is planned, the costs will be calculated by Institute grants management staff based on the recommendations outlined below in the COMMITTEE BUDGET RECOMMENDATIONS section.

RESUME AND SUMMARY OF DISCUSSION: This exceptional new application for a Mentored Clinical Scientist Research Career Development Award (K08) entitled The HIV Latent Reservoir, Suboptimal Immune Response on Antiretroviral Therapy, and Exogenous Cytokine Therapies was submitted by Johns Hopkins University, Baltimore, MD with Dr. Annukka Antar as the Principle Investigator (PI) and supported by Dr. Robert Siliciano as Primary Mentor and Drs. Richard Moore and Joel Blankson as co-mentors, Johns Hopkins University. Research proposed in this application seeks to determine if HIV latent reservoir (LR) size and inducibility are related to suboptimal immune responses and if cytokine therapies designed to increase CD4 counts also expand the LR. Results can generate information that can be used for development of HIV therapeutics.

The review committee identified many strengths in this application. This is a well-written application from a highly qualified candidate. There are strong and informative support letters that give further confidence that the candidate is exceptional and deserving of support. The career plan is well-aligned with the proposed research plan. The mentoring team is strong and can provide outstanding support for the candidate. The application describes interesting scientific and clinical questions and the available research environment will benefit her. The candidate appears to purposefully avoid overlapping with her co-mentors but might perhaps consider how her work is parallel and could extend their approaches.

There were a few minor weaknesses to this application identified by the review committee. Providing additional information about suboptimal immune responders present in cohorts would strengthened the application. There are concerns that Aim 3 appears to be tangentially related to Aims 1 and 2. There concern about the potential patient sample size for IL7 and IL15 treatments. The application does not appear to present data showing the intact proviral DNA assay (IPDA) can distinguish intact vs defective integrated virus. Moreover, validation of the IPDA does not appear to be presented.

In summary, the application has many strengths and a few weaknesses that only slightly reduce enthusiasm for the application.

Based upon the evaluation of scientific and technical merit, this application received an Overall Impact/Priority score of [redacted]

DESCRIPTION (provided by applicant):

A significant percentage of HIV-positive individuals who start antiretroviral therapy (ART) with a low CD4+ T cell count have CD4 counts that plateau at abnormally low levels despite years of virologic suppression on ART. The risk of death for these suboptimal immune responders (SoIRs) is 2-3 times higher than that of individuals whose CD4 count rises appropriately with ART, and this higher risk of death persists for a decade or more. The mechanisms underlying the suboptimal immune recovery and increased mortality rates in SoIRs remain poorly defined. One clear association has emerged: SoIRs have significantly higher levels of immune activation than other ART-treated individuals. We know that stimulation of HIV-infected CD4s through the T cell receptor results in HIV RNA and protein production and recognition by HIV-specific cytotoxic T lymphocytes. This suggests that the usual daily antigenic stimulation of CD4s could produce excess immune activation in individuals with a very large burden of latent HIV. Concordantly, a correlation between the frequency of infected CD4+ T cells and low CD4 counts on ART has been reported several times. However, these studies did not control for CD4 nadir or time on ART, so it is not clear whether SoIRs have a higher burden of infected CD4+ T cells. We hypothesize that increased induction from the HIV latent reservoir (LR), whether because of a larger LR size or increased inducibility from the LR, is correlated with suboptimal immune response. LR size and inducibility have never been simultaneously evaluated, but we will do so using efficient new assays that can discriminate intact from defective HIV proviruses. We will determine whether LR size and

inducibility contribute to suboptimal immune response and whether cytokine therapies designed to increase CD4 counts also expand the LR. For Aim 1, we will determine whether the size of the HIV LR in blood and lymphoid tissue is positively correlated with suboptimal immune response using the new intact proviral DNA assay (IPDA), a droplet digital PCR assay that separately quantifies intact and defective proviruses, on samples from SoIRs and age- and nadir-matched controls identified from within the ACTG Longitudinal Linked Randomized Trials study and three large cohorts in Baltimore, San Francisco, and Cleveland. For Aim 2, we will determine whether infected CD4+ T cells of SoIRs are more readily inducible from latency using a quantitative viral induction assay on blood samples from SoIRs and matched controls. For Aim 3, we will determine whether cytokine therapies that increase CD4 count also expand the HIV LR by using the IPDA to measure LR size in samples from clinical trials of exogenous IL-7, IL-15, and IL-2 in treated HIV. Through formal didactic training and structured mentorship from experts in HIV reservoirs, HIV immunology, clinical research, and biostatistics, the PI will develop a unique skillset in HIV latency techniques, immunological techniques and knowledge, statistics, and translational research. This training provides a pathway to an independent career as a translational investigator researching the contribution of viral factors to the pathogenesis of treated HIV.

PUBLIC HEALTH RELEVANCE

A significant percentage of HIV-positive individuals maintained on suppressive antiretroviral therapy have CD4 counts that plateau at abnormally low levels, and this population has a significantly higher rate of morbidity and mortality that persists for at least a decade after starting therapy. The mechanisms underlying this suboptimal immune recovery are poorly defined, but there is suggestive evidence that the induction of HIV from the latent reservoir is higher in this population. By determining whether LR size and inducibility contribute to suboptimal immune response and whether cytokine therapies designed to increase CD4 counts also expand the LR, this proposal will provide critical information that will aid in the development of therapeutics for this high-risk population.

CRITIQUE 1

Candidate:	[redacted]
Career Development Plan/Career Goals /Plan to Provide Mentoring:	
Research Plan:	[redacted]
Mentor(s), Co-Mentor(s), Consultant(s), Collaborator(s):	
Environment/Commitment to the Candidate:	[redacted]

Overall Impact:

The applicant is currently an infectious disease fellow in the laboratory of Dr. Robert Siliciano, Division of Infectious Diseases, John Hopkins University. Dr. Antar proposes to investigate potential viral and cellular mechanisms that may contribute to the lack of increased CD4 T cell levels over time in individuals that have low CD4 T cell levels at the start of ART, despite viral suppression during continued ART. The applicant also proposes to address changes in the latency reservoir in HIV-infected individuals treated with IL2, IL7, and IL15.

There are considerable strengths to the application, the highly-qualified applicant, the career plan, the interesting scientific and clinical questions posed, the mentor and the cutting-edge research environment of his laboratory. Selection of co-mentors and advisors, and the clinical cohorts from which all cellular samples will be obtained are strengths. However, there are some weaknesses with the application, such as the absence of preliminary data from her cohorts and the concern as to whether Aim 3 adds to the application. These weaknesses slightly dampened enthusiasm for the application.

1. Candidate:

Strengths

- The candidate is an infectious disease fellow in the laboratory of Dr. Robert Siliciano, Division of Infectious Diseases, John Hopkins University.
- She received a number of awards during her MD/PhD training at Vanderbilt and during her fellowship training at Hopkins.
- She has excellent training in virology from her PhD program with Dr. Dermody at Vanderbilt. and was productive during this time.
- The candidate is clinically well-trained, board certified in internal medicine and infectious disease and trained for 2 years as a hospitalist before starting her infectious disease fellowship training. Published case reports and opinion pieces during her clinical training.
- Excellent publications during her MD/PhD training period and has been productive during her fellowship period as a co-author.
- Dr. Anderson, Director, Johns Hopkins University Department of Medicine, and Dr. Thomas, Chief, Division of Infectious Diseases, have indicated that they are appointing her in a full-time position as an Assistant Professor in the Division of Infectious Diseases by July 2019.

Weaknesses

- A minor concern is the lack of significant publication(s) during the fellowship period as a first author.

2. Career Development Plan/ Career Goals & Objectives:

Strengths

- The PI's plan to become an independent translational investigator includes didactic course work, in immunology, biostatistics, computing, gene expression analysis, and clinical practices. This course work will be necessary for her proposed and future career and proposed studies. The technical training plan will ensure her success in undertaking the proposed studies.
- Grant writing and mentorship program proposed to ensure a successful transition from "K-to-R".
- Classes and training in mentoring.
- Proposed strategy for meeting presentations, manuscript submissions, and R01 submission during the 4th year of the K08. Proposes to apply for CFAR and other types of funding after year 2 of the K08.
- Proposes continued clinical training in infectious disease and weekly ID rounds.
- Will be appointed as an Assistant Professor in the Division of Infectious Diseases by July 2019 regardless of the K08 outcome.
- [redacted]

Weaknesses

- This is some concern that only 80% protected time during the first 1-2 years might not be sufficient to allow the PI's program to get off the ground.

3. Research Plan:

Strengths

- The PI proposes to investigate the viral and cellular mechanisms underlying suboptimal immune recovery observed in individuals that start with a low CD4 T cell count (<350uL) and with extended ART. Moreover, the CD4 T cell counts don't increase over time despite virologic suppression. These individuals are at a higher risk of death as compared to individuals in which CD4 T cells rise after ART. Understanding the mechanisms as to why CD4 T cells don't rise after ART-mediated viral suppression is of clinical and basic science significance and may provide therapeutic insights.
- Based on publications showing a higher proviral load in CD4 T cells of individuals with lower CD4 T cells, although on ART and virally suppressed, the PI's hypothesizes (Aim 1) that the size of the latent reservoir in blood and lymph nodes positively correlates with a suboptimal immune response. The PI proposes to determine latency sample size in blood and lymph node tissues of suboptimal immune response and control (individuals with rising CD4 T cells during ART) individuals. Sample sizes proposed are appropriate for the studies. Studies proposed have merit and are feasible.
- The plan (Aim 2) to evaluate whether CD4 T cells from suboptimal immune responders are more readily inducible from HIV latency as compared to controls (individuals with rising CD4 T cells during ART) has merit. Determining the ratio of functional (and activatable) to non-functional integrated provirus has merit. The Siliciano group has the methodology to obtain this information from CD4 T cells, therefore the studies appear feasible.
- Determine changes in the latency reservoir in individuals as the result of IL2, IL7, and IL15 cytokine treatment for CD4 T cell restoration.
- The PI will take advantage of PCR-based methods in use, in the Siliciano group, to determine functional and non-functional virus present in CD4 T cells and cell-based methods to determine activatable virus using QVIA.
- PBL samples are available from SCOPE, JHHCC, and CLIF clinical cohorts for the planned studies.

Weaknesses

- It wasn't directly stated as to the numbers of suboptimal immune responders present in the SCOPE, JHHCC, and CLIF clinical cohorts and their viral loads. It is reasonable to assume that this information may be available from the enrolled participants. Providing this information would have strengthen that application.
- The scientific and clinical rationales for Aims 1 and 2 are reasonable and have merit. However, Aim 3, although of scientific and clinical interest, appears to be tangentially related to Aims 1 and 2. There is some concern that the patient sample size for IL7 and IL15 treatments are limiting and underpowered.

- There is much discussion about the intact proviral DNA assay (IPDA) to distinguish intact vs defective integrated virus. However, there is no data showing the discrimination ability of the assay – this should have been shown.

4. Mentor(s), Co-Mentor(s), Consultant(s), Collaborator(s):

Strengths

- The PI's primary mentor, Dr. Siliciano, is an internationally renowned HIV research and a leader in the area of latency. He has provided a very strong letter of support detailing what is expect of the candidate and what he and his group will provide.
- Dr. Siliciano's group has developed many of the techniques that will be employed by the PI for her research program.
- Dr. Moore, co-mentor, has established HIV clinical cohort that will be utilized by the PI for her research project. He has provided a very strong letter of support detailing what he and his group will provide to ensure success of the candidate and of the proposed project.
- Dr. Blankson has provided a detailed letter of his contribution to the mentoring/training of Dr. Antar.
- The PI has enlisted a strong Advisory Committee of clinical and basic researchers that will provide access to clinical cohorts for the proposed studies, technical advice and support, and statistical advice.

Weaknesses

- None apparent.

5. Environment and Institutional Commitment to the Candidate: 1

Strengths

- Excellent. Strong letters of support from her mentor, Dr. Siliciano and Dr. Anderson, Director, Johns Hopkins University Department of Medicine, and Dr. Thomas, Chief, Division of Infectious Diseases, indicating both university and laboratory support.
- Hopkins has internationally renowned HIV clinical and basic research programs and virology/immunology programs.
- HIV cohorts from which the blood/cellular samples will be obtained have been described.

Weaknesses

- None noted.

CRITIQUE 2

Candidate:

Career Development Plan/Career Goals /Plan to Provide Mentoring:

Research Plan:

Mentor(s), Co-Mentor(s), Consultant(s), Collaborator(s):

Environment/Commitment to the Candidate:

Overall Impact:
The applicant is an outstanding young investigator with strong prior research training who now proposes a rigorous research training plan that is designed to develop the skills and experience need for her to become an independent investigator. Strengths of the application include the prior training and commitment of the applicant, an innovative research plan that has great potential to produce high impact results, an outstanding team of mentors and advisors who will each have unique contributions to career development of the applicant, and an outstanding environment and institutional commitment to the applicant. Very few weaknesses were noted.

1. Candidate:
Strengths

- Excellent prior research training.
- Very strong letters from the referees that attest to the applicant's prior accomplishments and potential for becoming a successful independent investigator.

Weaknesses

- The candidate is developing a record of peer reviewed publications with several papers in quality journals. Her single first author paper has a high impact. However, at this point in her career, after graduate school and completion of ID fellowship training, there is a minor concern about the number of expected first author publications.

2. Career Development Plan/ Career Goals & Objectives:
Strengths

- The career development is very well planned with clearly stated training objectives and metrics for measuring success.
- There appears to have been very thoughtful consideration by the candidate about the direction that she wants to take in her career, and the skills and experiences that she will need to get there.
- Course is appropriate for the applicants training needs.
- Milestones and timeline are clearly laid out including plans for development a future R01 application.

Weaknesses

- None noted.

3. Research Plan:
Strengths

- Innovative hypotheses that are clearly stated and supported by existing data.
- The research plan is well integrated with the overall career development plan.
- Potential for high impact to the field.
- Clear plans for how the research could lead to a future R01 application.

Weaknesses

- Requiring that the HIV viral load only be < 200 c/mL for 12 months would potentially include individuals with levels of viral replication that could influence the results and introduce heterogeneity. While occasional blips in viral load in a suppressed patient are likely of little consequence, individuals who have sustained viremia in the 100-200 c/mL range are likely to be much different and simple < 200 criterion does not distinguish between these possibilities. The fact that the ACTG uses <200 c/mL as measure to compare the efficacy of different antiretroviral regimens in clinical trials does not seem to be a strong rationale for the proposed study where the intent is to identify study individuals who do not have immune recovery despite strong antiviral suppression.
- The application does not include information about the validation of the IPDA as a measure of the latent reservoir and since the in-press paper that is referenced is not yet available, it is difficult to evaluate the appropriateness of this assay for the proposed work.

4. Mentor(s), Co-Mentor(s), Consultant(s), Collaborator(s):

Strengths

- Outstanding mentoring team with the complementary expertise needed for both the applicant's career development and successful completion of the research project.

Weaknesses

- None noted.

5. Environment and Institutional Commitment to the Candidate:

Strengths

- JHU provides an outstanding environment for the proposed research training.
- The institutional commitment to the applicant is particularly strong.

Weaknesses

- None noted.

CRITIQUE 3

Candidate:
Career Development Plan/Career Goals /Plan to Provide Mentoring: [redacted]
Research Plan:
Mentor(s), Co-Mentor(s), Consultant(s), Collaborator(s): [redacted]
Environment/Commitment to the Candidate: [redacted]

Overall Impact:

This is an outstanding K08 application from a truly promising candidate who is currently an ID fellow at Johns Hopkins (JHU) under the mentorship of Dr. R. Siliciano. The candidate has a long-running interest in virology research and a solid record of clinical and research productivity as demonstrated by high-quality publications since her doctoral work. The team of mentors is also outstanding and well-qualified to support the applicant's research and career goals. Career developmental plan is nicely laid

out with relevant details consistent with the research plan and goal. Research plan addresses important topic about suboptimal immune responders that is still poorly understood. Data generated from the study are highly likely to have direct significant impact on the efforts to improve the standard care of HIV patients. In summary, the application has many strengths and negligible weaknesses.

1. Candidate:

Strengths

- Undergrad from Harvard in Chemistry with magna cum laude.
- PhD research at Vanderbilt (mentor: Terence Dermody) on the identification of a reovirus receptor on endothelial cells and reverse genetics system for double stranded viruses to result in 2 Cell Host Microbe papers (one first author, another second author).
- Clinical training at Johns Hopkins in ID: exceptionally productive with publication of a chapter in an ID textbook, 2 op-ed articles on antimicrobial pricing and access (USA Today and Annals of Internal Medicine), 3 case reports, and 4 online modulates for HIV Guide.
- Research fellowship at the Siliciano lab: generating a large database of full-length HIV from longitudinal samples from HIV+ patients on long-term ART, learning deep sequencing techniques, [redacted]
  Results are presented in the Keystone meeting in 2017.
- Also involved in highly productive collaborations: co-author a recently accepted Nature paper to help clarify the controversial findings about HIV reservoir in CD32-positive vs-negative cells and first co-author another paper on K. pneumonia antibiotic resistance (J Antimicrobial Chemotherapy).

Weaknesses

- None noted.

2. Career Development Plan/ Career Goals & Objectives:

Strengths

- A well-thought-out career goal and developmental plan describing specific mentors and trainings to acquire a set of scientific and technical expertise that include innovative HIV latency assays, flow cytometry for analysis and cell sorting, statistics, bioinformatics, translational research with clinical cohorts, grant writing, leadership/mentoring, and clinical ID skills.
- Training modules take advantage of coursework that are offered by JHU and each is relevant to the applicant's research plan and career goal.
- Career goal milestones are sensible and should be readily achievable based on past and current productivity record.

Weaknesses

- None noted.

3. Research Plan:

Strengths

- Research plan is developed logically, guidance from the mentor is clearly evident, experimental design is in line with the mentor's expertise and resources, but the research niche is created with clear demarcation for the applicant's independent work.
- Research topic is highly pertinent and should have direct impact on the efforts to improve and optimize HIV therapy.
- Research plan focuses on suboptimal immune responders; addresses interesting and testable hypothesis (do latent reservoir size and inducibility positively correlate with suboptimal immune reconstitution?); utilizes innovative duplex-droplet digital PCR assays to detect intact vs defective HIV proviruses and quantitative induction assay to measure RNA transcripts in isolated CD4 T cells ex vivo and in vitro, takes advantage at least 4 large cohorts plus 5 cytokine therapy clinical trials.
- Three specific aims are proposed; each independent of the others. 1) Size of latent reservoir in SoIR subjects (<350 CD4 count after 5-yrs of ART and starting with CD4 count <200) vs subjects who achieve >500 CD4 count after 5-yrs of ART and starting from the same low <200 CD4 count; 2) Inducibility of latent reservoir in the two groups of subjects, and 3) Size of latent reservoir in subjects who receive cytokine therapy (IL-2, IL-7, IL-15).
- Cell number requirement and limitation are acknowledged; alternative plans are presented, while maintaining the use of only resting CD4 cells for input.
- Sex and age variables will be considered (>30% female and age-specific subsets), along with other possible disparate risk factors, by matching SoIR and controls for gender, age, race, HCV, CMV, and iv drug use.
- Preliminary data are presented to show the feasibility of each assay needed for the 3 aims.
- Power calculation is presented and takes into account the available or required sample sizes.

Weaknesses

- The capacity of the intact proviral DNA assay (IPDA) to distinguish intact vs defective constructs is limited by the dual primer/probe sets and may detect only a subset of all potentially defective constructs. Details of the assay are not available.

4. Mentor(s), Co-Mentor(s), Consultant(s), Collaborator(s):

Strengths

- Outstanding team of primary mentor (R. Siliciano) and co-mentors (R. Moore, J. Blankson) with complementary expertise pertinent to the proposed research plan.
- The primary mentor writes a very strong letter of support, providing specific information about the candidate's background and her current research projects in his lab.
- SAC members and collaborators are all well qualified and lend additional essential support by direct collaboration via clinical specimen provision.
- Very strong supportive letters from references and collaborators who know the applicant personally, although all reference letters are from JHU except for the one from T. Dermody (the applicant's PhD thesis advisor in Vanderbilt).

Weaknesses

- None noted.

5. Environment and Institutional Commitment to the Candidate:

Strengths

- JHU is an outstanding top-tier research institution that will be able to ensure the successful completion of the proposed research.
- The mentor's lab has research interest that is congruent with the applicant' application but is also separate to allow the applicant's independence.
- The mentor's lab is very well funded and has plenty resources to support the candidate's research and career goals.
- Institutional support is evident from the letter from ID Chief and Director of Dept of Med. The applicant is assured a full-time Assistant Professor position at the division of ID by July 2019, regardless of this application outcome. With the K08 award, she will have guaranteed 80% protected research time and 20% clinical time, without teaching or administrative requirements.

Weaknesses

- None noted.

THE FOLLOWING SECTIONS WERE PREPARED BY THE SCIENTIFIC REVIEW OFFICER TO SUMMARIZE THE OUTCOME OF DISCUSSIONS OF THE REVIEW COMMITTEE, OR REVIEWERS' WRITTEN CRITIQUES, ON THE FOLLOWING ISSUES:

PROTECTION OF HUMAN SUBJECTS (Resume): Code 10 NOT APPLICABLE

Projects to be undertaken with support of this training grant, which involve human subjects, must conform to the NIH policies on the protection of human subjects. Guidance can be found in PHS398 application materials and the NIH Office of Extramural Research web site http://grants.nih.gov/grants/policy/hs/index.htm.

DATA AND SAFETY MONITORING PLAN: NOT APPLICABLE

VERTEBRATE ANIMALS (Resume): Code 10 NOT APPLICABLE

Projects to be undertaken with support from this training grant, which involve vertebrate animals, must conform to the NIH policies on the humane care and use of laboratory animals. Guidance can be found in PHS398 application materials and the NIH Office of Extramural Research web site http://grants.nih.gov/grants/olaw/olaw.htm**.**

BIOHAZARD COMMENT: ACCEPTABLE

TRAINING IN THE RESPONSIBLE CONDUCT OF RESEARCH: ACCEPTABLE

Format: Face-to-face discussions among trainees, junior faculty, and senior faculty both via the Research Integrity Colloquia and the Department meeting on an RCR topic and via informal conversations with the applicant's mentor and co-mentors.

Subject Matter: The applicant's plan covers a variety of topics relevant to the responsible conduct of research, including: conflict of interest, policies regarding human subjects, mentor/mentee responsibilities, collaborative research, peer review, data acquisition and laboratory tools, management, sharing and ownership, research misconduct and policies for handling misconduct, responsible authorship and publication, the scientist as a responsible member of society, contemporary ethical issues in biomedical research, and environmental and societal impacts of scientific research.

Faculty Participation: Informal training from the applicant's primary mentor and two co-mentors whom are experienced basic, translational, and clinical investigators. Hopkins faculty will also lead the Research Integrity Colloquia and the Departmental meeting on RCR topics.

Duration: 8 contact hours of suggested instruction and will be spread over the 5-year award period.

Frequency: 2-3 formal contact hours per year and many informal contact hours per year of the award period, and complete recertification in the school of medicine.

FOREIGN INSTITUTION: NOT APPLICABLE

SELECT AGENTS: NOT APPLICABLE

RESOURCE SHARING PLANS: ACCEPTABLE

Data Sharing Plan Comments (if >$500,000/year): ACCEPTABLE

Sharing Model Organisms Comments: **NOT APPLICABLE**
Genomic Data Sharing (GDS) Comments: **NOT APPLICABLE**

AUTHENTICATION OF KEY BIOLOGICAL AND/OR CHEMICAL RESOURCES: **ACCEPTABLE**

BUDGET AND PERIOD OF SUPPORT: **ACCEPTABLE**
The budget was recommended as requested.

Footnotes for 1 K08 AI143391-01; PI Name: Antar, Annukka Aida Rose

NIH has modified its policy regarding the receipt of resubmissions (amended applications). See Guide Notice NOT-OD-14-074 at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-14-074.html. The impact/priority score is calculated after discussion of an application by averaging the overall scores (1-9) given by all voting reviewers on the committee and multiplying by 10. The criterion scores are submitted prior to the meeting by the individual reviewers assigned to an application, and are not discussed specifically at the review meeting or calculated into the overall impact score. Some applications also receive a percentile ranking. For details on the review process, see http://grants.nih.gov/grants/peer_review_process.htm#scoring.