SUMMARY STATEMENT

(Privileged Communication)

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PROGRAM CONTACT:
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Application Number: 1 R03 HG006029-01

Principal Investigator

SAGOFF, MARK PHD

Applicant Organization: UNIVERSITY OF MARYLAND COLLEGE PK CAMPUS

Review Group: ELS (O1)
Ethical, Legal, and Social Implications of Human Genetics Study Section

Meeting Date: 06/07/2010
Council: OCT 2010
Requested Start: 01/01/2011

RFA/PA: PA08-013
PCC: X5JM

Project Title: Ecological Concepts of Human Identity in Microbiome and Metagenomic Research

SRG Action: Priority Score

Human Subjects: 10-No human subjects involved

Animal Subjects: 10-No live vertebrate animals involved for competing appl.

Project Year	Direct Costs Requested
1	50,000
2	50,000
TOTAL	100,000

DC Recommended

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.

1R03HG006029-01 SAGOFF, MARK

RESUME AND SUMMARY OF DISCUSSION: The investigators propose to assess use philosophical analysis to explore the ecological concepts, metaphors, and analogies that are beginning to frame our understanding of the human microbiome and to challenge entrenched mechanistic concepts of the human body and the human being. The potential to influence medical and public health ethics by providing an integrated or revised conceptual framework for conceiving of the human being/person is great. Thus the significance and potential impact of the project is very high. There are additional strengths to this application. The application is exceptionally well written and represents innovative, cutting edge thinking in the philosophy of biology. In addition, the philosophical, conceptual, historical, and ethical/normative analytical methods proposed are appropriate. The investigator has excellent qualifications for the work and he has put together an impressive, multidisciplinary advisory board, although during the discussion, it was pointed out that the advisory board could use more microbiome researchers. Overall, the Study Section was extremely enthusiastic about this application and its chances to develop a new ways of thinking about genetic causation.

DESCRIPTION (provided by applicant): The proposed research seeks to contribute to an emerging literature that assesses the philosophical implications of the ecological concepts, metaphors, and analogies that are beginning both to frame our understanding of the human microbiome and to challenge entrenched mechanistic concepts of the human body and the human being -- entrenched concepts that not only include the "blueprint" analogies of the Human Genome Project but stretch back at least to the discovery of the circulation of the blood. The proposed research will use philosophical analysis to explore and assess in the context of the Human Microbiome Project the application of ecological metaphors - such as "community," "superorganism," "homeostasis" "ecosystem," "dynamics," "complexity," etc. - to public and scientific understanding of such concepts as the "human body," the "human being" and the "human individual." The project acknowledges well-known problems in the ecological sciences that beset and may, indeed, defeat the application of concepts that attempt to unite organisms into natural systems and communities. The research proposed here will explore whether these kinds of problems also complicate the application of ecological concepts in the study of the human microbiome and metagenome. The proposed research will examine how normative concepts, such as "structure," "function," "interdependence," "community," and even "system" have moved back and forth between the medical and ecological sciences. It will discuss moral and conceptual implications of ecological images of the human individual - for example, the picture of the individual as a composite of microbial and human cells, the representation of the human genome as a kind of landscape, and the idealization of the microbiome as a kind of mixmaster of human and microbial traits. The proposed project will produce published papers and conference presentations that will help scientists concerned with the microbiome and metagenome to understand the ecological framework in which they may set their research.

PUBLIC HEALTH RELEVANCE: Public health research now presses on the frontiers of the human microbiome and metagenome but lacks a conceptual framework to integrate these microbial and genetic landscapes into recognizable images of the human being, the person, and the individual. By assessing through philosophical analysis emerging ecological concepts, metaphors, and an analogies in terms of which scientists frame their research, the proposed project will help clarify the goals of the Human Microbiome Project (HMP) in its relation to conceptions the patient and patient health the HMP seeks to serve.

CRITIQUE 1:

Significance: **4**
Investigator(s): 2

Innovation: 1
Approach: 2
Environment: 1

Overall Impact

Strengths:

- Examining new/emergent relationships between core concepts in ecology and medical genetics, an understudied area of conceptual analysis.
- Very innovative topic of study that is especially timely in light of new developments in the study of the human microbiome and NIH support of the Human Microbiome Project.

Weaknesses:

- Not clear what the analysis proposed would yield in terms of new philosophical insights, in large part because of the novelty of the topic.
- It is doubtful that the project will produce any translational/practical products of importance in the design and conduct of future studies of the human microbiome.

1. Significance

Strengths:

- The historical/conceptual studies proposed are extremely novel and represent "leading edge" thinking in the philosophy of biology. These studies have the potential to advance our thinking about the relationships among "human individuals" and the microbiota that exist in symbiotic relationship with humans.
- By elucidating unspoken ontologies at work in the rhetoric of contemporary genetics, the analysis proposed also may inform our thinking about major developments in human genetics, especially the increasingly common rejection of individualistic/atomistic discourse and naïvely deterministic views of genetic causation.

Weaknesses:

- The practical utility of the conceptual analyses proposed is unclear.
- How the investigator will translate key findings into monographs and panel presentations targetted to geneticists is also unclear.

2. Investigator(s)

Strengths:

- The PI is an established investigator who is trained in philosophy. His writing focuses on topics in philosophy of biology, ecology, and the ethics of genetic research.
- The PI is very well positioned, almost uniquely well positioned, to tackle the issues described in the application.
- The PI appears to have generated a great deal of interest in his work, as reflected in numerous letters of support from (uncompensated) experts in related studies.
- The PI has assembled a group of relevant experts to serve as advisors to the study. These advisors will bring additional areas of methodological and topical expertise to the project.

Weaknesses:

- The PI does not appear to have extensive ties to the ecology community, one of the two primary areas of study that he proposes to examine.

3. Innovation

Strengths:

- The PI is one of a handful of individuals interested in how normative categories/concepts from the ecological sciences may be shaping the development of studies in genetics. He has reached out to some of the other leading voices in this area and will work with them in examining this largely unexamined area of study.

Weaknesses:

- The philosophical methods are not innovative but are appropriate.

4. Approach

Strengths:

- Will draw on perspectives from history/philosophy of biology.
- Exceptionally well written background section demonstrates the investigator's mastery of this material.

Weaknesses:

- Plans for translating this work into more practical products are lacking (e.g. other than presenting papers at professional conferences and publishing a collection of articles, how will the PI disseminate key findings to researchers studying the human microbiome?).
- Historical themes/perspectives were less well developed in the project description, which focused primarily on philosophical analyses.

5. Environment

Strengths:

- The University of Maryland is an ideal place in which to perform these studies. Expertise can be found locally in the type of applied philosophical analysis proposed, as well as in human microbiome research.
- The PI has shared interests and a strong collegial relationship to researchers involved with the Human Microbiome Project, Drs. Fraser-Liggett and Ravel.

Weaknesses:

- None.

Protections for Human Subjects:

Not Applicable (No Human Subjects)

- OK as described.

Data and Safety Monitoring Plan (Applicable for Clinical Trials Only):

Not Applicable (No Clinical Trials)

Inclusion of Women, Minorities and Children:

Vertebrate Animals:

Not Applicable (No Vertebrate Animals)

Biohazards:

Not Applicable (No Biohazards)

Resubmission:

Renewal:

Revision:

Budget and Period of Support:

Recommend as Requested

Select Agents:

Not Applicable (No Select Agents)

Applications from Foreign Organizations:

Not Applicable (No Foreign Organizations)

Resource Sharing Plans:

Not Applicable (No Relevant Resources)

CRITIQUE 2:

Significance: 1
Investigator(s): 1
Innovation: 2
Approach: 2
Environment: 1

Overall Impact

Strengths

- The potential to exert strong influence on the intellectual development of an emerging field is great.
- The target audience for products of this project—a book and conference presentations—is appropriate. The goal is not to transform policy or revolutionize scientific practice, but to influence how scientific analyses are interpreted and thus, to some degree, the research agenda surrounding the microbiome. The proposed analysis has the potential to do this.

Weaknesses

- Engagement with more key microbiome investigators would help to ensure that maximal impact was achieved within the relevant scientific sub-community. There is some representation of the microbiome research community on the partial list of advisory panel members; however, the addition of others—if they are truly committed to the project—would strengthen its impact in that community.

1. Significance

Strengths

- The proposed analysis addresses at a conceptual and normative level an emerging area of bioscience.
- The potential to influence medical and public health ethics by providing an integrated or revised conceptual framework for conceiving of the human being/person is great. The critical analysis to be provided may indicate a revised agenda for bioethical/medical ethics analysis by necessitating a rethinking of genetic, environmental, social, political contributions to disease and disability.

Weaknesses

- None.

2. Investigator(s)

Strengths

- The PI is highly qualified and productive; moreover, he has demonstrated productive collaborative relationships with several of the advisory panel members.
- Those comprising the advisory panel bring important expertise to the critical conceptual and normative analysis proposed.

Weaknesses

- None.

3. Innovation

Strengths

- This project in innovative in redressing a lack of interaction between ecology theorists and clinical and human biology investigators/theorists.
- It is innovative in reconceptualizing connections between the environmental, public health, medical/clinical ethics domains.
- It is innovative for its focus on the human microbiome, which is itself an emerging domain of investigation.
- It is innovative for integrating historical and philosophical methods/analyses along these dimensions and for considering the implications for both conceptual and normative/ethical analysis.

Weaknesses

- None.

4. Approach

Strengths

- The philosophical, conceptual, historical, and ethical/normative analytical methods proposed are entirely appropriate.
- The use of an advisory panel, co-thinkers on these issues, will enhance the analysis of a well-qualified PI.
- If the PI brings to the project and its products the same clarity of explanation that was evident in the proposal's explanation of the conceptual conundrums, the analyses should be clear and highly useful.

Weaknesses

- None.

5. Environment

Strengths

- Adequate.

Weaknesses

Protections for Human Subjects:

Not Applicable (No Human Subjects)

Data and Safety Monitoring Plan (Applicable for Clinical Trials Only):

Vertebrate Animals:

Not Applicable (No Vertebrate Animals)

Biohazards:

Not Applicable (No Biohazards)

Applications from Foreign Organizations:

Not Applicable (No Foreign Organizations)

Select Agents:

Not Applicable (No Select Agents)

Resource Sharing Plans:

Not Applicable (No Relevant Resources)

Budget and Period of Support:

Recommend as Requested

CRITIQUE 3:

Significance: 3
Investigator(s): 2
Innovation: 3
Approach: 3
Environment: 2

Overall Impact

Strengths

- This is a philosophical project that seeks to ponder how we conceptualize and understand ourselves in light of the microbiome, which is an important challenge in light of the revelations of the Microbiome Project.
- The PI is a well-respected bioethicist with significant experience as the director of the Institute for Philosophy and Public Policy at the U. of Maryland.
- While this is an R03, the PI has assembled an impressive, multidisciplinary advisory team.
- The P.I. has significant experience in this field.
- The project proposes to develop novel ways of conceptualizing and understanding humanity in light of unfolding knowledge about the human microbiome.
- The Institute for Philosophy and Public Policy at the U. of Maryland seems well-suited for this project.

Weaknesses

- There is an odd observation (p. 29) that seems to say that the microbiome will not change our current conceptions of humanity and then suggests that we need to development additional conceptualizations, without explaining why we need to do this.

Protections for Human Subjects:

Not Applicable (No Human Subjects)

Data and Safety Monitoring Plan (Applicable for Clinical Trials Only):

Inclusion of Women, Minorities and Children:

Vertebrate Animals:

Not Applicable (No Vertebrate Animals)

Biohazards:

Not Applicable (No Biohazards)

Budget and Period of Support:

Recommend as Requested

THE FOLLOWING RESUME SECTIONS WERE PREPARED BY THE SCIENTIFIC REVIEW OFFICER TO SUMMARIZE THE OUTCOME OF DISCUSSIONS OF THE REVIEW COMMITTEE ON THE FOLLOWING ISSUES:

COMMITTEE BUDGET RECOMMENDATIONS: The budget was recommended as requested.

NOTICE: In 2008 NIH modified its policy regarding the receipt of resubmission (formerly termed amended) applications. Detailed information can be found by accessing the following URL address: http://grants.nih.gov/grants/policy/amendedapps.htm