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TITLE: Prevalence and Seroconversion of IgE to the mammalian oligosaccharide galactose-α-1,3-galactose and relationship to comorbid disease in military personnel

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The oligosaccharide galactose-α-1,3-galactose (α-Gal) is a blood group-like antigen of non-primate mammals and is the causal epitope in an IgE-mediated allergic disorder called the α-Gal syndrome. Ingestion of red meat and other products derived from mammals (e.g., dairy) can lead to allergic manifestations including hives, swelling, abdominal cramping, and anaphylaxis with a characteristic delay of 3-6 hours in subjects who are sensitized to α-Gal. An additional feature that distinguishes α-Gal syndrome from traditional food allergies is that sensitization to α-Gal is caused by tick bites, specifically bites of *Amblyomma americanum* (the lone star tick) in the United States. This study's purpose is to utilize the Department of Defense Serum Repository to investigate the prevalence and incident seroconversion of α-Gal specific IgE, the blood marker for α-Gal syndrome, in banked serum from active military personnel who were stationed at installations where the lone star tick is common (i.e., select bases in the Southeast and coastal Atlantic). Additionally, we will relate these findings with the clinical record of the service members over a ten-year time window to determine whether IgE to α-Gal is associated with reported allergic, gastrointestinal, cardiovascular symptoms of disease and other medical conditions. All regulatory approvals have been obtained and the study is awaiting shipping of serum samples from the DoD Serum Repository to University of Virginia.

15. SUBJECT TERMS

NONE LISTED

16. SECURITY CLASSIFICATION OF: unclassified			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
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1. **INTRODUCTION:** *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

The oligosaccharide galactose-α-1,3-galactose (α-Gal) is a blood group-like antigen of non-primate mammals and is the causal epitope in an IgE-mediated allergic disorder called the α-Gal syndrome. Ingestion of red meat and other products derived from mammals (e.g., dairy) can lead to allergic manifestations including hives, swelling, abdominal cramping, and anaphylaxis with a characteristic delay of 3-6 hours in subjects who are sensitized to α-Gal. An additional feature that distinguishes α-Gal syndrome from traditional food allergies is that sensitization to α-Gal is caused by tick bites, specifically bites of *Amblyomma americanum* (the lone star tick) in the United States. This study's purpose is to utilize the Department of Defense Serum Repository to investigate the prevalence and incident seroconversion of α-Gal specific IgE, the blood marker for α-Gal syndrome, in banked serum from active military personnel who were stationed at installations where the lone star tick is common (i.e., select bases in the Southeast and coastal Atlantic). Additionally, we will relate these findings with the clinical record of the service members over a ten-year time window to determine whether IgE to α-Gal is associated with reported allergic, gastrointestinal, cardiovascular symptoms of disease and other medical conditions

2. **KEYWORDS:** *Provide a brief list of keywords (limit to 20 words).*

Alpha-gal, meat allergy, lone star tick, α-Gal syndrome

3. **ACCOMPLISHMENTS:** *The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.*

What were the major goals of the project?
List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

1. Acquire regulatory approval and transfer samples to UVA allergy laboratory.
   Target date: 01 May 2020 Completion date: Not completed
2. Conduct IgE assays and share data with investigators.
   Target date: 01 Mar 2021 Completion date: Not completed
3. Analysis of data and manuscript preparation.
   Target date: 31 Aug 2022 Completion date: Not completed

What was accomplished under these goals?
For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

Under Major Task 1 the following subtasks were completed: Local IRN approval, USAMRA HRPO approval, Data Sharing Agreement completion with Defense Health Agency and the Armed Forces Health Surveillance Branch.

No other subtasks or major tasks have been accomplished.

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

Nothing to Report

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Nothing to Report

What do you plan to do during the next reporting period to accomplish the goals?
If this is the final report, state "Nothing to Report."

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

We have all regulatory approvals, support agreements, contract, and financial account transferred to the appropriate parties. The next step relies on the Armed Forces Health Surveillance Branch to identify appropriate subjects per the inclusion and exclusion criteria and transfer the samples to University of Virginia.

4. **IMPACT:** D*escribe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:*

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

Nothing to Report

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to Report

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to Report

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to Report

5. **CHANGES/PROBLEMS:** *The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:*

Three major challenges have affected the timeline of our project.

1. Worldwide pandemic of COVID-19
   The DoD serum to be utilized in for the study are supplied by the DoD Serum Repository which is managed by the Armed Forces Health Surveillance Branch (AFHSB). The AFHSB is the central epidemiologic resource for the U.S. Armed Forces, conducting medical surveillance for DoD members. With the onset of COVID-19 the AFHSB has had to shift resources away from routine studies to urgent COVID-19 surveillance.
2. Delay in obtaining the Data Sharing Agreement with the Defense Health Agency.
   Obtaining the DSAs simply took longer than anticipated. This has been resolved.
3. Delay in transfer of payment for serum samples to the AFHSB/DoD Serum Repository
   There was confusion over expectation of O&M funds vs. RDT&E funds and how to transfer the funds to AFHSB. This has been resolved.

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

Overall the study is currently delayed by four months. The AFHSB anticipates being able to proceed serum sample subject identification and shipping in approximately 3 weeks. We anticipate we will be able to recover the study delays during the serum sample and analyses major task periods.

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

A delay in meeting SOW milestones has bed to less costs than anticipated at this point in the study. We anticipate utilizing these funds once the study proceeds.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

None

Significant changes in use of biohazards and/or select agents

None

6. **PRODUCTS:** *List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."*

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

  Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to Report

  Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to Report

  Other publications, conference papers and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

Nothing to Report

- **Website(s) or other Internet site(s)**
  List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to Report

- **Technologies or techniques**
  Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.

Nothing to Report

- **Inventions, patent applications, and/or licenses**
  Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to Report

- **Other Products**

  Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:

  - *data or databases;*
  - *physical collections;*
  - *audio or video products;*
  - *software;*
  - *models;*
  - *educational aids or curricula;*
  - *instruments or equipment;*
  - *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
  - *clinical interventions;*
  - *new business creation; and*
  - *other.*

Nothing to Report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change".

Example:

Name:	*Mary Smith*
Project Role:	*Graduate Student*
Researcher Identifier (e.g. ORCID ID):	*1234567*
Nearest person month worked:	*5*
Contribution to Project:	*Ms. Smith has performed work in the area of combined error-control and constrained coding.*
Funding Support:	*The Ford Foundation (Complete only if the funding support is provided from other than this award.)*

Name:	Cade Nylund
Organization:	Uniformed Services University of the Health Sciences
Project Role:	Principle Investigator
ORCID:	0000-0003-4543-6804
Nearest Person-month worked:	2-3
Contribution to Project:	Principle Investigator

Name:	Jeffrey Wilson
Organization:	University of Virginia
Project Role:	Co-Investigator/ UVA Site Director
ORCID:	0000-0002-5975-1760
Nearest Person-month worked:	~1
Contribution to Project:	Co- Investigator, administrative preparation, preparing lab, ordered and set up lab: IgE machine and reagents.

Name:	Apryl Susi
Organization:	Henry Jackson Foundation
Project Role:	Co-Investigator
ORCID:	0000-0003-2580-2563
Nearest Person-month worked:	3
Contribution to Project:	Co-Investigator, coordination of IRB, contracts, DSSA, support agreements etc.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

No change in support for senior/key personnel at USUHS.

Dr. Jeffrey Wilson's obtained a new American Academy of Allergy Asthma & Immunology faculty development award. No scientific overlap.

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.

Provide the following information for each partnership:
Organization Name:
Location of Organization: (if foreign location list country)
Partner's contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other.*

Organizational Name: The University of Virginia
Location of Organization: Charlottesville, VA
Partner's Contribution to the Project: Collaboration

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: *For collaborative awards, independent reports are required from BOTH the Initiating Principal Investigator (PI) and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to* ***https://ers.amedd.army.mil*** *for each unique award.*

QUAD CHARTS: *If applicable, the Quad Chart (available on https://www.usamraa.army.mil) should be updated and submitted with attachments.*

9. APPENDICES: *Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.*