**AWARD NUMBER:** W81XWH-18-2-0033

**TITLE:** Objective Assessment of Auditory Pathway Integrity and Functional Hearing Abilities

**PRINCIPAL INVESTIGATOR:** Kenneth W. Grant, PhD

**CONTRACTING ORGANIZATION:** The Geneva Foundation

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**PREPARED FOR:** U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

# REPORT DOCUMENTATION PAGE

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**4. TITLE AND SUBTITLE**
Objective Assessment of Auditory Pathway Integrity and Functional Hearing Abilities

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**6. AUTHOR(S)**

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**5e. TASK NUMBER**

**5f. WORK UNIT NUMBER**

**7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)**

The Geneva Foundation
917 Pacific Ave, Suite 600
Tacoma, WA 98402

**8. PERFORMING ORGANIZATION REPORT**

**9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)**

U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

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**13. SUPPLEMENTARY NOTES**

**14. ABSTRACT**
In preparation for imminent hair cell regeneration clinical trials, it is essential to develop a systematic approach to assess the degree of functional hearing restoration as the regeneration of hair cells, the reintegration of these cells and their associated neural pathways within the auditory system, and the reorganization of the auditory cortex to newly restored sound inputs progresses over time. Therefore, the purpose of developing a functional assessment battery is to provide multiple opportunities to demonstrate success, from early physical reintegration of the cochlea through the thalamus-cortical pathway (such as tests of outer and inner hair cell, brainstem, and efferent system activity), to simple and more complex sound discrimination crucial for understanding speech in noisy environments. To demonstrate the utility of this functional assessment battery, listeners with a wide range of hearing loss from normal hearing to moderate-to-severe hearing loss will evaluated to establish expected values for different degrees of hearing damage. To validate the repeatability of the functional assessment battery, a subset of listeners with varying degrees of hearing loss will be tested on multiple occasions. Finally, the extent to which simple and complex pre-attentive discrimination abilities, as well as cochlear reintegration measures, can predict complex speech in noise performance will be evaluated.

**15. SUBJECT TERMS**

**NONE LISTED**

| **16. SECURITY CLASSIFICATION OF:** | | | **17. LIMITATION OF ABSTRACT** | **18. NUMBER OF PAGES** | **19a. NAME OF RESPONSIBLE PERSON** |
|---|---|---|---|---|---|
| **a. REPORT** | **b. ABSTRACT** | **c. THIS PAGE** | | | USAMRMC |
| Unclassified | Unclassified | Unclassified | Unclassified | 15 | **19b. TELEPHONE NUMBER** *(include area code)* |

## TABLE OF CONTENTS

1. **INTRODUCTION:** *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

The U.S. involvement in Iraq and Afghanistan has resulted in unprecedented amounts of trauma to the auditory system. This damage may manifest itself in patients complaining of difficulty understanding speech in complex backgrounds while at the same time presenting with normal to near-normal audiometric thresholds. Standard clinical audiometric tests fail to properly diagnose the true extent of hearing damage, and current rehabilitation strategies may not restore hearing to a functioning status appropriate for military readiness. To address this problem, biotechnology companies are working on techniques to restore hearing through regeneration of cochlear hair cells. This research project seeks to develop and validate an objective battery of tests to track the various stages of reintegration and reorganization necessary to restore hearing to a functional state appropriate for active-duty service.

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

Hearing loss, hearing restoration, electroencephalography

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.*

**Aim 1:** Identify objective pre-attentive and unbiased measures that differentiate between normal hearing systems and those with auditory dysfunction and establish expected values of those measures for varying degrees of hearing loss. (Months 1-18)

- **Major Task 1.1:** Finalize all hires (completed 12/27/2018). Replace Dr. Rebecca Lewis (completed 08/10/2020). Obtain IRB approval (completed 10/14/2018). Program and pilot all test measures. (completed 6/26/2020)
- **Major Task 1.2:** Administer the proposed test battery to the three hearing groups to compare results that likely represent stages of incremental improvement during hearing restoration. (initiated 2/3/2020)

**Aim 2:** Assess differences between individual's objective test measures between sessions to determine reliability of the test measure. (15% complete via pilot testing)

- **Major Task 2.1:** Re-administer the proposed test battery to a subset of participants from the three hearing groups at multiple time periods to determine within-subject differences. (not yet initiated)

**Aim 3:** Evaluate the ability to predict functional measures of speech in noise performance from objective measures of the physical integrity of the auditory system. (ongoing)

- **Major Task 3:1** Determine the minimum number of tests necessary to provide adequate information about the comprehensive functionality of the entire auditory pathway for clinical feasibility. (ongoing)

**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.*

Computer programming and initial pilot testing has been completed. Since the last reporting period, we have received and been able to set up the ER10X system from Dartmouth to measure the middle-ear-muscle reflex (with modifications). We are currently working on resolving processing issues in the system's output.

Participant recruitment and enrollment was initiated February 2020. Currently 3 people have completed the protocol and 3 potential participants are scheduled in the coming weeks. Dr. Rebecca Lewis has decided to leave the project and has taken a full-time research audiologist position in California. We have hired a replacement, Dr. Ian Phillips, who joined our team as a Research Scientist on August 10th, 2020 and is currently undergoing the onboarding process. At this early stage of development, no data are yet available. Despite a 3 ½ month suspension of face-to-face research activities due to the COVID-19 pandemic, we have experienced a steady flow of volunteer interest in the study and expect this trend to continue for the remainder of the study.

Major regulatory activities to date:

- IRB approval was obtained October 14, 2018
- The CRADA between Geneva and Walter Reed was established in January 2019.
- HRPO approval was obtained on January 24th, 2019.
- Continuing review for 2020 was approved on August 11th, 2020
- Data sharing agreement with CNRM was established in July 2020

**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

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

During the next reporting period we will continue to recruit and enroll participants. Retesting of a subset of participants to determine within-subject differences will also begin. Lastly, the data sharing agreement with the US Army Office of The Surgeon General (OTSG) / Medical Command (MEDCOM) will be established.

***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:*

Nothing to Report

**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.*

Participant enrollment began February 2020. However, due the COVID-19 pandemic, face-to-face research activities were suspended from March 17th, 2020 to July 6th, 2020. Despite the unexpected interruption, we have experienced a steady flow of interested volunteers for study participation since the return of face-to-face activities. At this time, we are unsure if an extension will be required to compensate for COVID related delays.

Dr. Lewis has begun a new position as a research audiologist in California. Dr. Phillips, our new Research Scientist joined the team on August 10th and will be in charge of running the study. While Dr. Myers continues to handle regulatory matters and assist in participant recruitment/enrollment, she will be leaving her position as program manager in late September/early October. Inquiries to fill the position when Dr. Myers leaves have been employed.

**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.*

Personnel turnover and delays in programming equipment have contributed to slower expenditures than originally predicted; however, the biggest impact on expenditures has been the suspension of face-to-face research activities due to the COVID-19 pandemic. As a result, recruitment and enrollment of participants was suspended from March 17th, 2020 until July 6th, 2020. However, since recruitment has resumed, we have observed a steady flow of interested volunteers.

**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**

Nothing to Report

**Significant changes in use or care of vertebrate animals**

Nothing to Report

**Significant changes in use of biohazards and/or select agents**

Nothing to Report

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 |
  |---|

-

*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: | Kenneth Grant |
| No change | |
| Name: | Rebecca Lewis |
| No change | |
| Name: | Jennifer Myers |
| No change | |
| Name: | Ian Phillips |
| No change | |
| Name: | Sandeep Phatak |
| No change | |
| Name: | Scott Bressler |
| No change | |

**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.*

| |
|---|
| Nothing to Report |

**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:*
*<u>Organization Name:</u>*
*<u>Location of Organization: (if foreign location list country)</u>*
*<u>Partner's contribution to the project</u> (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.*

Walter Reed National Military Medical Center (WRNMMC)

| | |
|---|---|
| Organization Name: | The Center for Neuroscience and Regenerative Medicine (CNRM) |
| Location of Organization: | Rockville, MD |
| Partner's contribution to the project: | In-Kind Support. Under this collaboration, the project uses CNRM for recruitment purposes (data sharing agreement established July 2020) |

US Army Office of The Surgeon General (OTSG) / Medical Command (MEDCOM)

| | |
|---|---|
| Organization Name: | US Army Office of The Surgeon General (OTSG) |
| Location of Organization: | San Antonio, TX |
| Partner's contribution to the project: | In-Kind Support. Data sharing agreement in progress for cognitive assessment data on borrow equipment. |

Dartmouth College

| | |
|---|---|
| Organization Name: | Dartmouth |
| Location of Organization: | Hanover, NH |
| Partner's contribution to the project: | In-Kind Support. Loaner agreement established to borrow equipment. |

## 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.*