AWARD NUMBER: W81XWH-20-1-0484, RH190022

TITLE: Toward a Self-Administered Hearing Protection Regimen **PRINCIPAL**

INVESTIGATOR: Donna S. Whitlon, Ph.D.

CONTRACTING ORGANIZATION: Northwestern University

REPORT DATE: OCTOBER 2021

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Development Command

Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;

Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
OCTOBER 2021	Annual	30SEPT2020 - 29SEPT2021

4. TITLE AND SUBTITLE

Toward a Self-Administered Hearing Protection Regimen

5a. CONTRACT NUMBER
W81XWH-20-1-0484

5b. GRANT NUMBER
RH190022

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

Donna S.Whitlon, Ph.D.

E-Mail: whitlon@northwestern.edu

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

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

Northwestern University
633 Clark Street
Evanston, IL 60208

8. PERFORMING ORGANIZATION REPORT NUMBER

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

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

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

This project aims to further both our basic understanding of the effects of different oral statins, with and without steroid drugs, on hearing loss and to compare the ability to protect hearing with the ability to protect hair cells and synapses within the cochlea. Concomitant with the laboratory studies, we are undertaking a small, innovative clinical trial to determine if the prevailing treatment (steroids) of idiopathic sudden sensorineural hearing loss can be improved by adding a short course of statins. Despite equipment failure of our original equipment and delays in the supply line due to manufacturing and COVID, we acquired our new sound booth and stand, ABR/OAE setup, noise speaker, laptop and software to run the system, oscilloscope, noise generator, and amplifier. We created a new type of mouse cage in order to be able to expose control and experimental animals simultaneously. We have validated, by dose-response, the noise exposure on noise-induced hearing loss in mice and have initiated our proposed laboratory studies. In anticipation of our clinical trial, we created and had approved our clinical protocol by the local IRB and the Army and have listed it on ClinicalTrials.gov.

15. SUBJECT TERMS

Noise induced hearing loss, Statins, Sudden Sensorineural Hearing Loss, Clinical Trial

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	7	19b. TELEPHONE NUMBER *(include area code)*

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

TABLE OF CONTENTS

1. INTRODUCTION

This project aims to further both our basic understanding of the effects of different oral statins, with and without steroid drugs, on hearing loss, and to compare the ability to protect hearing with the ability to protect hair cells and synapses within the cochlea. Concomitant with the laboratory studies, we are undertaking a small, innovative clinical trial to determine if the prevailing treatment (steroids) for idiopathic sudden sensorineural hearing loss can be improved by adding a short course of and oral statin.

2. KEYWORDS

Noise induced hearing loss, statins, Sudden sensorineural hearing loss, steroids, clinical trial

3. ACCOMPLISHMENTS

- **What were the major goals of the project?**

	Percent Complete
Acquire IACUC approval and ACURO approval	100%
Validate new ABR measuring equipment	100%
Measure additional ABR of statins	initiated
Statistics on ABR holds	x
Immunolabel all cochleas, count HC and synapses Statistics (above ABR study)	initiated
ABR study of Statin and Steroid and controls	x
Immunolabel all cochleas, count HC and synapses, statistics (statin+steroid ABR study)	X
Acquire Human Subjects Approval	100%
Acquire HRPO approval	100%
Hire and train clinical coordinator, put patient questionnaires on line, set up clinic for study	X
Set up drugs at the pharmacy	X
Initate clinical trial, acquire data, calculate results	X
Begin writing paper on clinical Trial	X
Final calculations and final paper writing	x

- **What was accomplished under these goals?**

1) <u>Major Activities</u>
   Acquire all of the equipment necessary for carrying out auditory brain stem response measurements (ABR) on mice.
   Validate the effects of noise on mouse hearing loss and compare to the data acquired previously
   Begin examination of hair cells and synapses in experimental and control cochleas

Create all the documents necessary for our Clinical Trial, acquire approval from our Institutional Review Board for Human subjects (IRB) and from the Army.

2) Specific objectives

Validate the frequency spread and intensity of the noise from the new speaker setup.
Carry out a noise dose-response experiment on the mice to determine the best intensity for our noise experiments and how that compares to our prior noise experiment,
Reproduce a prior experiment with oral lovastatin.
Take appropriate courses and acquire certificates for Clinical Trials.
Write detailed clinical trial procedure and associated documents such as Informed Consent, advertising, etc,
Have the Clinical Trial documents approved by the Institutional Review Board and the Army.
List the clinical trial on ClinicalTrials.gov
Determine the most appropriate statin to use in the clinical trial

3) Significant results or key outcomes

The equipment we had been using for ABR studies before we were able to set up our new equipment for the current project, began to deliver inconsistent results. Delivery of our new equipment was significantly delayed in manufacturing and supply line due to COVID. We have now been able to collect all the necessary equipment and set up and validate our new ABR setup. We have acquired for this system a new sound booth and stand, ABR/OAE setup, noise speaker, laptop, software to run the system, oscilloscope, noise generator, and amplifier. We are borrowing two other functional pieces of equipment (a noise filter and a microphone). We created a new mouse cage to be able to expose control and experimental animals simultaneously. We can generate an 8-16 kHz noise exposure at 110 dB SPL similar to that we used in past work, and we have validated, by dose-response, that, as before, the best noise exposure for our experiments is 110 dB SPL x 2 hours. We are now initiating our proposed laboratory studies. Immunolabeling and confocal microscopy of cochleas -hair cells and synapses – is ongoing. Our Clinical Trial has been approved by the IRB and the ARMY and is listed on ClinicalTrials.gov.

4) Goals not met

We are delayed in carrying out our laboratory studies. Since the clinical trial depends on those studies, the recruitment of our first patients on the study will be delayed January 2022. Due to COVID and the necessity to keep the laboratory uncrowded, we also delayed in hiring new employees.

- **What opportunities for training and professional development had the project provided?**
  Nothing to Report

- **How were the results disseminated to communities of interest?**
  Nothing to Report

- **What do you plan to do during the next reporting period to accomplish the goals**?
  To carry out all the ABR studies proposed as well as the histological assessment of the cochlea, we will hire additional laboratory associates.
  Studies of different oral statins will be evaluated as a protection from noise induced hearing loss in mice.
  The clinical trial will be initiated.

4. IMPACT

- **What was the impact on the development of the principal discipline(s) of the project?**
  Nothing to report
- **What was the impact on other disciplines?**

Nothing to report

- **What was the impact on technology transfer?**

  Nothing to report
- **What was the impact on society beyond science and technology?**
  Nothing to report

5. CHANGES/PROBLEMS:

- **Changes in approach and reasons for Change**
  Nothing to report
- **Actual or anticipated problems or delays and actions or plans to resolve them**
  To get back on our time schedule with the screening of statins for the clinical trial, we will test them only for 1 week after noise exposure instead of two weeks. There is very little difference in ABR (if any) between 1 week after noise exposure and 2 weeks. This will allow us more throughput with the animals. We are already able to test 8 per set rather than 6 due to the change in cages. We are also carrying a control for each noise exposure in order to know immediately if there is any problem with our setup, to shorten the time for troubleshooting any problems.
  We will hire assistants for ABR and for the cochlear dissections-histology.
  We will hire a Clinical Coordinator and have that person take the clinical coordinator course from Northwestern.
  Once the statin to use in the clinical trial is determined, this will be adjusted in the IRB and Army approval forms (currently it lists all statins), and the statins+placebo will be made and set up by the Investigational Pharmacy.
- **Changes that had a significant effect on expenditures**
  COVID requirements – thinning the density of employees, even a hiring freeze for a few months, had us delay hiring of necessary staff.
  The delay in hiring, delayed our experiments and therefore our expenditures.
- **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents.**
  Nothing to report.

6. PRODUCTS

Nothing to report

7. PARTICIPANTS AND OTHER COLLABORATING ORGANIZATIONS

- **What individuals have worked on the project**

Name	Donna S Whitlon	Claus-Peter Richter	Fred Depreux	Lyubov Czech
Project Role	PI	Co-Investigator	Sr. Research Associate	Research Tech II
Researcher Identifier				
Nearest Person-Month worked	4.8	1.2	6	6
Contribution to Project	Experimental design, troubleshooting	Auditory physiology (ABR) and equipment advice and troubleshooting	ABR studies	Immunohistochemistry, Confocal microscopy and counting of hair cells and synapses

- **Has there been a change in the active other support of the PD/PI or senior/key personnel since the last reporting period?**
  Nothing to report
- **What other organizations were involved as partners?**
  Nothing to report