

AWARD NUMBER: W81XWH-19-1-0339

TITLE: Enhanced Melanoma Vaccine Against Neoantigens and Shared Antigens by CD40 Activation and TLR Agonists

PRINCIPAL INVESTIGATOR: Dr. Brian Gastman, MD

CONTRACTING ORGANIZATION: The Cleveland Clinic Foundation, Cleveland, OH

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TYPE OF REPORT: Annual Report

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

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14. ABSTRACT This project will test the hypotheses that vaccination with CD40 Ab/TLR3 agonist is safe and induces strong and durable T cell responses to the peptides in the vaccine, and that a mutated neoantigen peptide (BRAF585-614-V600E) is immunogenic. There have been no findings during this reporting period as the study is not yet open at our site.						
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1. INTRODUCTION:

This project will test the hypotheses that vaccination with CD40 Ab/TLR3 agonist is safe and induces strong and durable T cell responses to the peptides in the vaccine, and that a mutated neoantigen peptide (BRAF585-614–V600E) is immunogenic.

2. KEYWORDS:

Melanoma, Vaccine, Peptides, Local adjuvants

3. ACCOMPLISHMENTS:

What were the major goals of the project?

Aim 1. To test the safety and immunogenicity of vaccination against melanoma with helper peptides + CD40 antibody CDX-1140 + TLR3 agonist polyICLC.

Aim 2. To determine whether vaccination with peptides in CDX-1140 + polyICLC enhances dendritic cell activation and maturation, Th1 dominant microenvironment, and induces tertiary lymphoid structures (TLS).

Aim 3: To evaluate whether vaccination against a mutant BRAF peptide induces T cells that recognize BRAF-mutant melanomas, infiltrate nevi and are associated with regression of nevi.

What was accomplished under these goals?

- 1) Synthesis of new peptide for the proposed vaccine: neoAg-mBRAF. This peptide, representing a mutated sequence in BRAF-V600E, was synthesized in a GMP laboratory and received in October 2019.
- 2) Determine optimal conditions for solubilization of neoAg-mBRAF peptide.
- 3) Sterile filtration and vialing of the neoAg-mBRAF peptide (600 vials) in our new GMP laboratory at the University of Virginia. December 2019.
- 4) Submitted vials of neoAg-mBRAF for quality assurance testing including mass spectrometry (for accurate mass and amino acid sequence), amino acid analysis (for concentration of peptide), HPLC (for purity), sterility testing. These all met target thus far. Sterility testing results are expected before end of February, which will complete those tests.

FINALIZATION OF CLINICAL TRIAL PROTOCOL (Mel66 protocol) AND HRPO REVIEW

- 5) Revised and completed clinical trial protocol that forms the basis of this project.
- 6) Submitted protocol to HRPO for pre-review 9/26/19
- 7) Guidance from HRPO pre-review provided 12/19/19
- 8) We submitted the protocol and associated requested documents to HRPO 1/3/20 for full review - HRPO Log Number E00804.1a
- 9) The revised research protocol and supportive documents received by the USAMRDC ORP HRPO on 3 January 2020 were reviewed. On 31 January 2020, we were authorized to proceed with the FDA and IRB submissions.
- 10) Site initiation visit occurred 7/15/2021.

DRAFTING OF IND APPLICATION TO THE FDA

- 11) We have been given approval by the FDA to submit an amendment to our existing IND application for the addition of the neoAg-mBRAF peptide and the clinical trial protocol for this project.
- 12) A draft of that IND application has been completed. Final edits are in process, including the lot release data for the neoAg-mBRAF peptide.

CONTRACTING WITH CELLDLEX FOR USE OF THEIR CDX-1140 ANTIBODY

- 12) Contract with Celldex written and approved for use of their CDX-1140 antibody in this clinical trial.
- 13) Material transfer agreement written and approved with Celldex for provision of a sample of the CDX-1140 antibody for preclinical testing to ensure that it remains functional when mixed with polyICLC and peptides. The CDX-1140 antibody was received in the laboratory at the end of January 2020.
- 14) Deeming trial feasible for our site/ beginning trial start-up phase
- 15) Deemed feasible 7/21/2020
- 16) Submitted to Cleveland Clinic IRB on 10/14/2020

What opportunities for training and professional development has 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?

Site activation to occur by end of August 2021.

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

Nothing to report.

Changes that had a significant impact on expenditures

Nothing to Report

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

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:

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

Journal publications.

Nothing to Report

Books or other non-periodical, one-time publications.

Nothing to Report

Other publications, conference papers and presentations.

Nothing to Report

- **Website(s) or other Internet site(s)**

<https://clinicaltrials.gov/ct2/show/NCT04364230?term=mel66&draw=2&rank=1>

- **Technologies or techniques**

Nothing to Report

- **Inventions, patent applications, and/or licenses**

An invention disclosure has been submitted to the UVA Licensing and Ventures group for the vaccine preparation including the new neoAg-mBRAF peptide plus 6 other melanoma helper peptides.

The neoAg-mBRAF peptide has been prepared as a clinical-grade reagent under GMP conditions.

- **Other Products**

Nothing to Report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: Brian Gastman, MD
Project Role: PI
Researcher Identifier (e.g. ORCID):
Nearest person month worked: 1
Contribution to Project: Dr. Gastman has overseen and been intimately involved with the protocol writing and revision and contracts, selecting the vendor to synthesize the neoAg mBRAF peptide, determining the optimal solubilization of the neoAg mBRAF peptide. Drafted SOP for GMP solubilization and vialing of neoAg mBRAF peptide.

Name: Mark Lennon and Kelly Shepherd
Project Role: Research Coordinators
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 1
Contribution to Project: Mr. Lennon and Kelly Shepherd have worked on the regulatory startup for this project.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to Report

What other organizations were involved as partners?

*Organization Name: **University of Virginia***

*Location of Organization: (if foreign location list country) **Charlottesville, VA***

*Partner's contribution to the project (identify one or more) Sponsor/ Collaboration:
Craig Slingluff, MD (Initiating PI) W81XWH-19-1-0338*

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS:

QUAD CHARTS:

9. APPENDICES: