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TITLE: Effects of Passive Immunization on Immunogenicity of Filovirus Vaccines

PRINCIPAL INVESTIGATOR: Steven B. Bradfute, Ph.D.

CONTRACTING ORGANIZATION: University of New Mexico Health Sciences Center

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The overall research idea of this proposal is to ascertain the feasibility of providing short-term protection against Ebola virus infection while co-administering Ebola virus vaccines to provide long-term protection against disease. Ebola virus vaccine candidates (a live replicating vesicular stomatitis virus (VSV) expressing Ebola-GP and a replication-deficient adenovirus (AdV) expressing Ebola GP) have been used in humans. For therapeutic purposes, monoclonal antibodies (ZMapp, mAb114) and antiviral small molecules (Remdesivir) are also being tested in human infections. However, neither antibody therapy nor small molecule inhibitors of Ebola virus replication will protect against infection long-term, and vaccines do not provide immediate protection. To that end, this proposal will test multiple strategies to combine therapeutic drugs with vaccines to generate rapid short-term as well as long-term protection against Ebola virus. In the first and second year we found that administration of neutralizing antibodies had an effect on the short-term immunogenicity of both VSV and AdV vaccines and that VSV elicited substantially higher IgG titers than AdV vaccine. In year three, we found there was no significant impact on antibodies elicited by VSV vaccine after treatment with the antiviral small molecule remdesivir. Ongoing studies in the no-cost-extension phase of the work will assess impact of co-administration of vaccines with antibodies or antivirals on animal survival in live-virus challenge models.

15. SUBJECT TERMS

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REPORT OUTLINE

- **INTRODUCTION:** Ebola virus causes severe disease and often death in human infections. Recent large outbreaks have demonstrated that the virus is a serious emerging threat to human health. The overall research idea of this proposal is to ascertain the feasibility of providing short-term protection against Ebola virus infection while co-administering Ebola virus vaccines to provide long-term protection against disease. Two Ebola virus vaccine candidates, a live vesicular stomatitis virus expressing Ebola glycoprotein (VSV-GP) and a single-cycle adenovirus vector expressing Ebola glycoprotein (AdV-GP) have been extensively tested in humans, and the VSV-GP has been used as a ring vaccine in Ebola virus outbreaks. The use of monoclonal antibodies has been very promising in nonhuman primate studies and have been used experimentally in human infections, as have the small molecules Favipiravir (T-705) and Remdesivir (GS-5734). However, neither antibody therapy nor small molecule inhibitors of Ebola virus replication will protect against infection long-term, and vaccines do not provide immediate protection. What is needed for military personnel and health care workers responding to filovirus outbreaks is a regimen to protect in the short-term against infection, and in the long-term as well. To that end, this proposal will test multiple strategies to combine therapeutic drugs with vaccines to generate rapid short-term as well as long-term protection against Ebola virus. Specific Aim 1 is to test the effects of time of administration of Ebola virus neutralizing antibody cocktails on immunogenicity of advanced Ebola virus vaccines, and to test how these regiments affect the neutralizing antibody cocktail levels. Specific Aim 2 is to determine whether functional non-neutralizing anti-GP antibodies, and selective anti-sGP antibodies, affect vaccine immunogenicity. Specific Aim 3 was initially designed to compare the effects of Remdesivir and Favipiravir administration on vaccination, although we have submitted an IACUC protocol amendment to replace Favipiravir with Molnupiravir. This report focuses on Year 3 of this grant, which comprises Specific Aim 3.

- **KEYWORDS:** Ebola, virus, vaccination, vaccine, filovirus, antibody, monoclonal, therapeutics, drugs, Remdesivir, Favipiravir, Molnupiravir, ZMAPP, mAb114, glycoprotein, MIL77, GP.

- **ACCOMPLISHMENTS:**
  - **What were the major goals of the project?**
    - Major Task 1: Determine whether antivirals effective against Ebola virus affect vaccine immunogenicity.
      - Subtask 1: Determine effects of Remdesivir on vaccine immunogencity
        - 50% accomplished
      - Subtask 2: Determine the effects of Favipiravir on vaccine immunogenicity
        - IACUC amendment submitted to replace Favipiravir with Molnupiravir
      - Subtask 3: Assessment of protection against live virus challenge
        - Delayed due to COVID-19
      - Milestone 1: Establishment of optimal regimen for administering Ebola vaccines and non-neutralizing antibodies
        - 50% accomplished
  - **What was accomplished under these goals?**

a) Major activities

Acquisition of Ebola virus vaccines. We acquired the VSV-GP vaccine through the generosity of Dr. Heinz Feldmann and used this for the mouse experiments. However, we were not able to acquire the ChAd3-GP vaccine, as it is being used in clinical trials and we were not given permission to acquire this vaccine. We therefore contracted the generation of a replication-defective AdV5-GP vaccine, since no ChAd3 backbone was commercially available. We screened several AdV serotype 5-GP viruses by western blot and picked a clone that expressed GP at a high level. We received virus at 5 x 1012 particles/mL, sufficient for the in vivo experiments.

Acquisition of Ebola virus antivirals. The goal of this aim was to test how Ebola virus vaccines are impacted by concurrent and offset timed treatments with established and potential Ebola antiviral drugs, remdesivir and molnupiravir. Remdesivir and was acquired from MedChemExpress, and reconstituted according to manufacturer's instructions. Originally, favipiravir was to be tested; however, clinical trials conducted after the beginning of this project suggested that favipiravir was not protective in humans. Therefore, we have submitted an IACUC amendment to replace this drug with molnupiravir, which has protective qualities against SARS-CoV-2 in humans and decreases Ebola virus replication in vitro.

Assessment of the effects of antiviral treatment on Ebola virus vaccine immunogenicity. The results of these experiments are described in subsection c below.

Continued assessment of the effects of vaccination on Ebola virus vaccine immunogenicity and the effects of vaccines on monoclonal antibody persistence. The results of these experiments are described in subsection c, "Continuation of major task 1" below.

b) Specific objectives

The specific objectives of this year were:

<u>Major Task 1: Determine whether antivirals effective against Ebola virus affect vaccine immunogenicity.</u>

Subtask 1: Determine effects of Remdesivir on vaccine immunogenicity (Months 24-28)

Subtask 2: Determine effects of Favipiravir [replaced by molnupiravir] on vaccine immunogenicity (Months 24-28)

Subtask 3: Assessment of protection against live virus challenge

c) Significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative)

Major Task 1: Determine whether antivirals effective against Ebola virus (EBOV) affect vaccine immunogenicity

Subtask 1: Determine effects of Remdesivir on vaccine immunogenicity

Methods. BALB/c mice (n=5 per group) were vaccinated intramuscularly with either 2 x 10^4 pfu of VSV-GP or mock vaccinated (as a negative control) on day 0. Remdesivir was formulated in 12% sulfobutylether-beta-cyclodextrin in water at a pH of 3.0 and injected intravenously through the ocular vein (10 mg/kg) daily for 10 days, beginning on day -2, day 0, or day +2, or injected with diluent only as a negative control. Antibody assays (both ELISA and functional assays) will be performed on sera isolated on days 5, 10, 14, 21, 42, and 63. Mice were bled via the submandibular route on days 5, 10, 14, 21, 42, and 63 to assay for vaccine-induced antibody responses. ELISAs were conducted on a 1:40 dilution of sera for anti-Ebola GP IgG and IgM mouse antibody for days 5, 10, 14 and 21 (Figure 1). In addition, Ebola virus GP1,2-specific T cell responses from spleen and mesenteric lymph nodes will be measured on day 63 as in Aim 1 to determine effects of the small molecules on vaccine-induced immune responses.

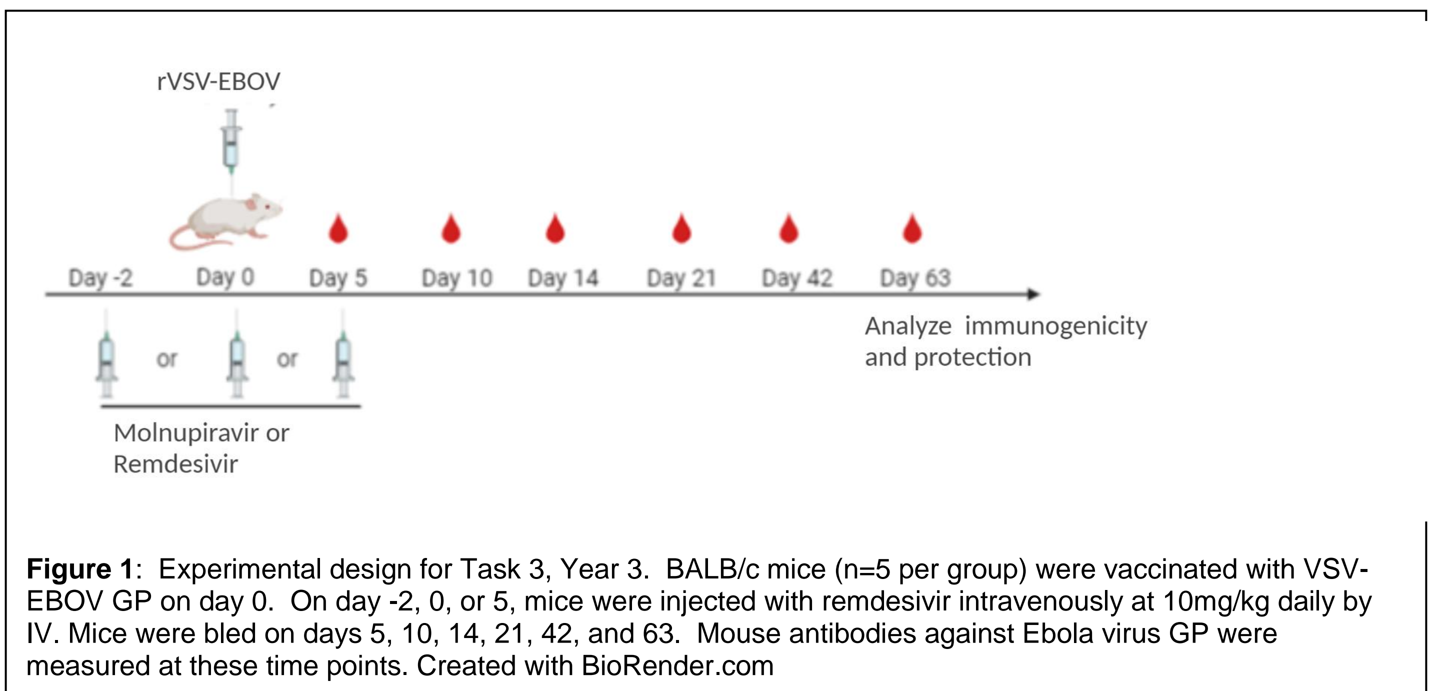

Figure 1: Experimental design for Task 3, Year 3. BALB/c mice (n=5 per group) were vaccinated with VSV-EBOV GP on day 0. On day -2, 0, or 5, mice were injected with remdesivir intravenously at 10mg/kg daily by IV. Mice were bled on days 5, 10, 14, 21, 42, and 63. Mouse antibodies against Ebola virus GP were measured at these time points. Created with BioRender.com

Statistical analysis. Antibody levels were compared to vaccine-only groups with vaccine+antibody groups using a one-way ANOVA with Dunnett's multiple comparisons test. A p value of <0.05 was considered to be significant.

Results.

rVSV-EBOV GP vaccination with remdesivir IV treatment

IgG/IgM titers after VSV-GP vaccination.

Mice receiving VSV-GP on day 0 and treated with Remdesivir on days -2, 0, or 5 were bled on days 5, 10, 14 and 21. As IgM has been shown to be a major contributor to VSV-GP-generated functional antibodies[1] ELISAs were

performed with the sera to assay both IgG and IgM levels. Early total IgG/IgM titers were assayed to determine whether the concurrent, prior or delayed antiviral treatment resulted in a delay of the establishment of antibodies against EBOV GP compared to the control vaccine-only animals.

On day 5, there was a mouse IgM/IgG anti-Ebola GP response detected by ELISA in the rVSV-EBOV GP vaccinated group, There were no significant differences in mock IV and the Day -2 and Day 0 Remdesivir treatments. However, there is a significant difference at Day 5 between the mock IV and the Day 3 Remdesivir,

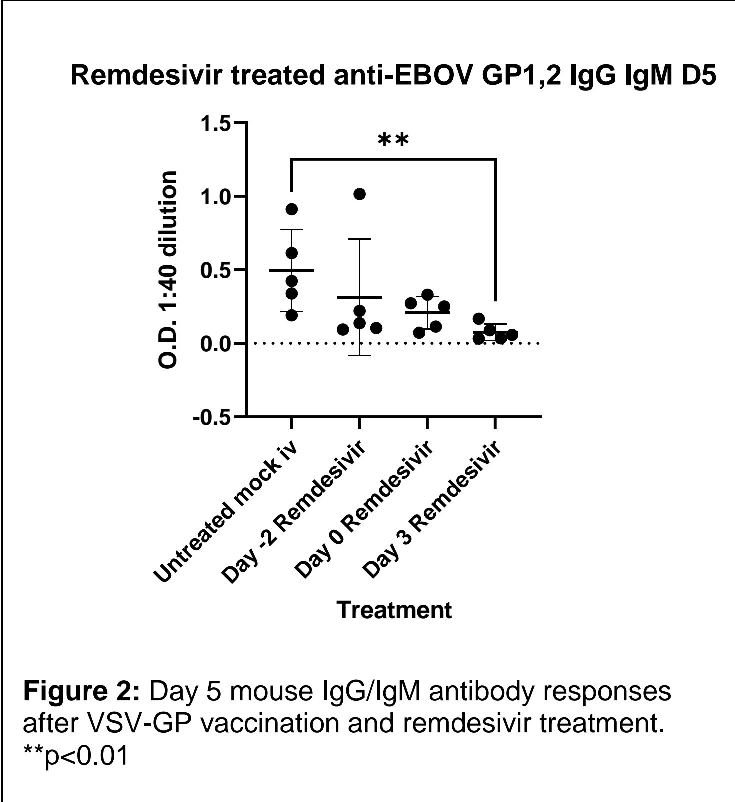

Figure 2: Day 5 mouse IgG/IgM antibody responses after VSV-GP vaccination and remdesivir treatment. **p<0.01

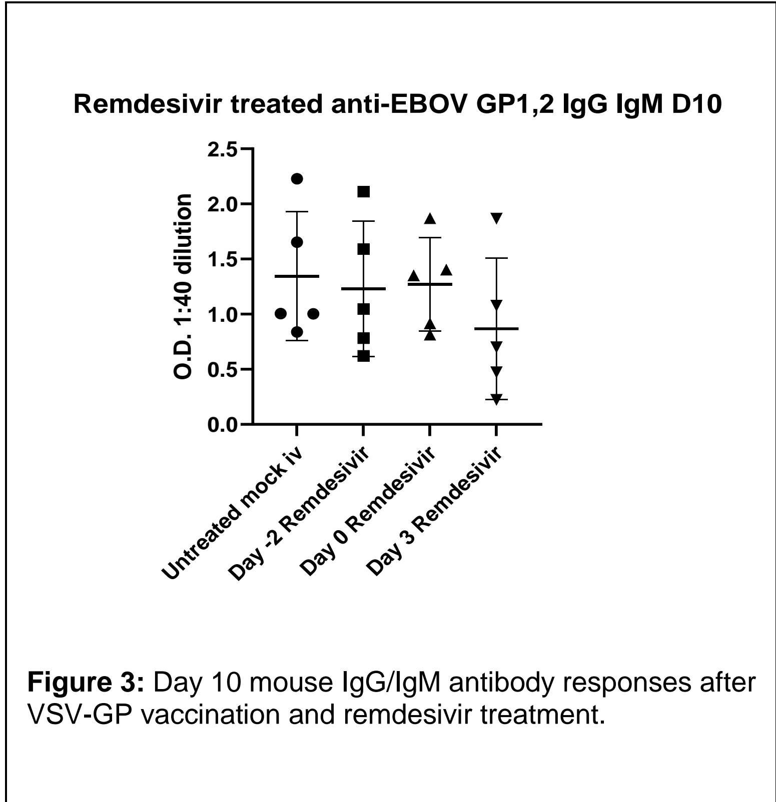

Figure 3: Day 10 mouse IgG/IgM antibody responses after VSV-GP vaccination and remdesivir treatment.

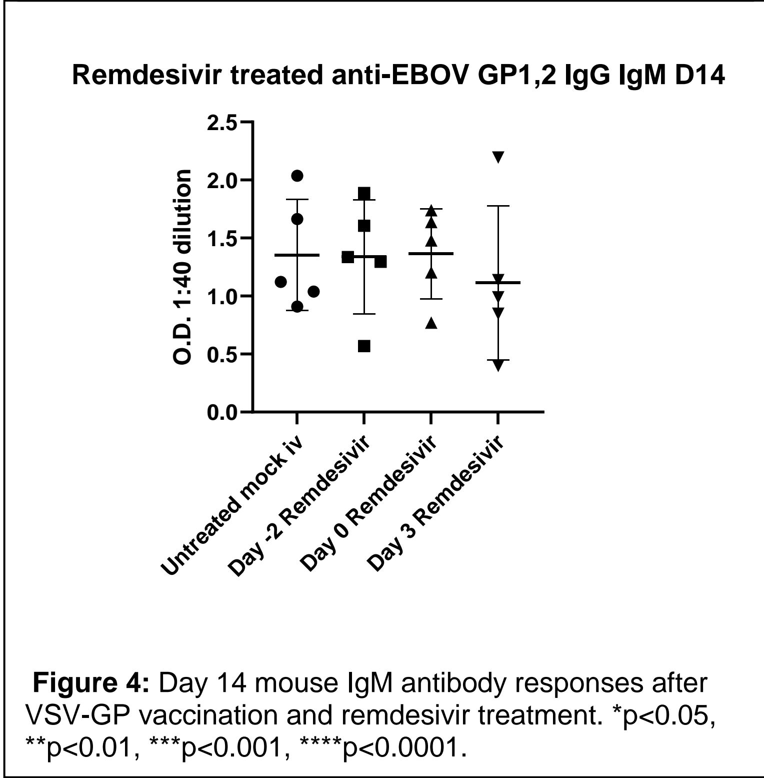

Figure 4: Day 14 mouse IgM antibody responses after VSV-GP vaccination and remdesivir treatment. *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001.

which did not receive any IV, vehicle or drug, prior to day 3. This may suggest there is an increase in titers in response to the IV injection itself after vaccination, rather than a suppression of the vaccine-induced titers in response to Remdesivir treatment, as no suppression is seen in the day -2 and day 0 treated groups. The mock IV group vehicle IVs were identical in timing to the Remdesivir Day -2 treated group, and so by day 5, both the Remdesivir day -2 and the mock IV group had received the same number of IV injections (6), whereas the day 3 had only received 3. The theory that titers are increased after mock IV injections is further supported by the increased titers in the mock IV group compared the mock oral gavage group (Figure 2 and data not shown), which both received the same intramuscular vaccination of rVSV-EBOV GP and no drug. In the future, a control group of mock IV mice at the same as each of the treated groups could account for this difference.

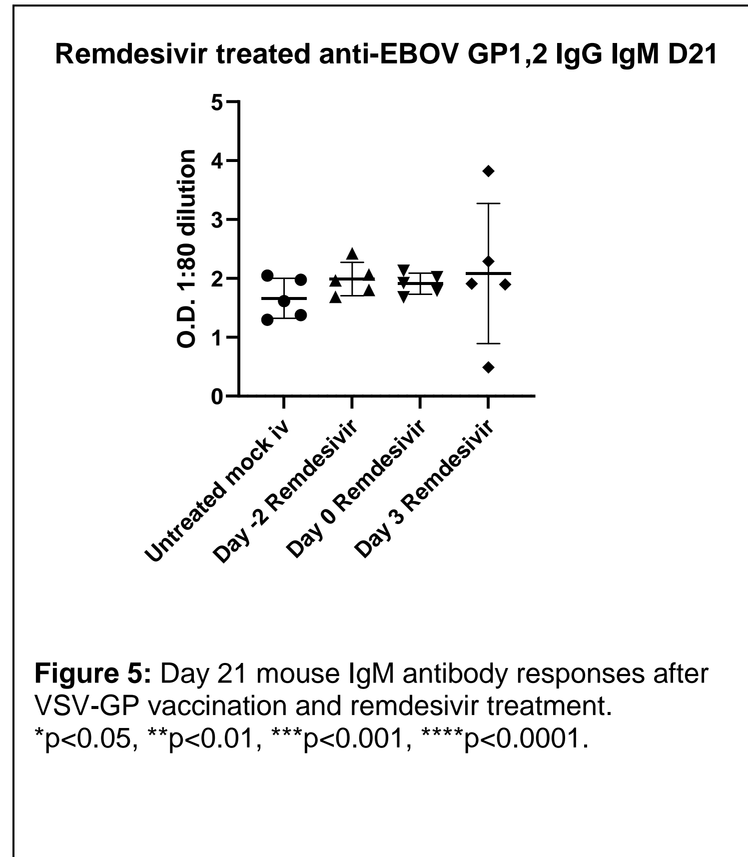

Figure 5: Day 21 mouse IgM antibody responses after VSV-GP vaccination and remdesivir treatment. *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001.

At day 10, significant IgG/IgM titers were present in the rVSV-EBOV GP vaccine only group and all three of the Remdesivir treated groups, although there are no significant differences in titer (Figure 3). On day 14, there are still no significant differences between the rVSV-EBOV GP vaccine only group and all three of the Remdesivir treated groups, but there is a trend that the Day 3 Remdesivir has lower titers than the mock IV and Day -2 Remdesivir group (Figure 4). The trend may also be accounted for by the differences in IV injections after vaccination. There do not appear to be any differences between the untreated mock IV and the Day -2 Remdesivir titers at day 10 or day 14.

By day 21, there are no significant differences between any of the Remdesivir-treated groups and the untreated group that received the mock IV (Figure 5). It appears that any trend showing a decrease in titer in the groups that received later IV has disappeared, and by Day 21 all the groups have received 10 IV injections. As expected, the titers of antibodies continue to increase from day 5 to day 21, and the total IgG/IgM antibody is higher at day 21.

Subtask 2: Determine effects of molnupiravir (EIDD- 2801) on vaccine immunogenicity

The original proposal was to test favipiravir, a then promising antiviral against Ebola. However, since the original grant was summited, multiple reports suggesting the limited efficacy of favipiravir as an in vivo antiviral against Ebola virus infection have emerged, including a retrospective study that revealed that the effect on mortality of favipiravir treatment in humans was not statistically significant[2]. Due to these findings, we plan to alter the original proposal to instead investigate molnupiravir (Merck's Lagevrio), an antiviral that was approved in December 2021 for use in against SARS-CoV-2 in the COVID-19 pandemic[3]. Molnupiravir has been shown to be an effective antiviral in vitro against Ebola virus[4]. However, it is possible that molnupiravir could inhibit the VSV replication and thus diminish efficacy of rVSV-EBOV-GP vaccination. This possibility is supported by published findings that a molnupiravir derivative (4'fluorouridine (EIDD-2749)) blocks VSV replication *in vitro*[5]. Therefore, there is a need to assess *in vivo* effects of molnupiravir on rVSV-EBOV GP vaccination. We have submitted an IACUC amendment to add molnupiravir to these studies; upon approval, we will submit an amended ACURO protocol for inclusion of molnupiravir in these studies in the no cost extension period.

Continuation of Major Task 1 from Year 1: Test the effects of time of administration of Ebola virus neutralizing antibody cocktails on immunogenicity of advanced Ebola virus vaccines
Subtask 1: Determine the effects of timing of passive neutralizing antibody administration on vaccine immunogenicity

Methods. BALB/c mice (n=5 per group) were vaccinated intramuscularly with either 2 x 10^4 pfu of VSV-GP or mock vaccinated (as a negative control) on day 0. The MIL77 cocktail or mAb114 was injected intravenously

with 100 ug of each antibody treatment on days -2, 0, and +5 (as a control, for each vaccine one group was vaccinated but not injected with antibody). Neutralizing antibody titers were measured against Ebola virus using VSV expressing luciferase and carrying Ebola GP in place of VSV-G.

Statistical analysis. Antibody levels were compared to vaccine-only groups with vaccine+antibody groups using a one-way Anova with Dunnett's multiple comparisons test. A p value of <0.05 was considered to be significant.

Results.

After improving the assay to test the neutralizing titers of the serum antibodies, we were able to test day 63 serum from the co-administration of neutralizing antibody cocktails and Ebola virus vaccines. Figure 6 shows the neutralizing antibody titers in response to VSV vaccination with no antibodies, or with mAb 114 or MIL 77 at either day -2, 0 or day 5. There is a clear trend suggesting that the prior treatment with either mAb 114 or MIL77 reduces the amount of neutralization. The lower luciferase values indicate more rVSV-EBOV GP neutralization has occurred, as less rVSV-EBOV GP is able to enter the cells and produce luciferase. These results align with the previous results from day 42 ELISAs (Figure 7) that suggested higher total IgG titers in the rVSV-EBOV GP vaccine only group, compared to the groups that received the neutralizing antibodies prior to vaccination. The mAb 114 delivered at day 5 also has very good neutralization with a low average and small range of results.

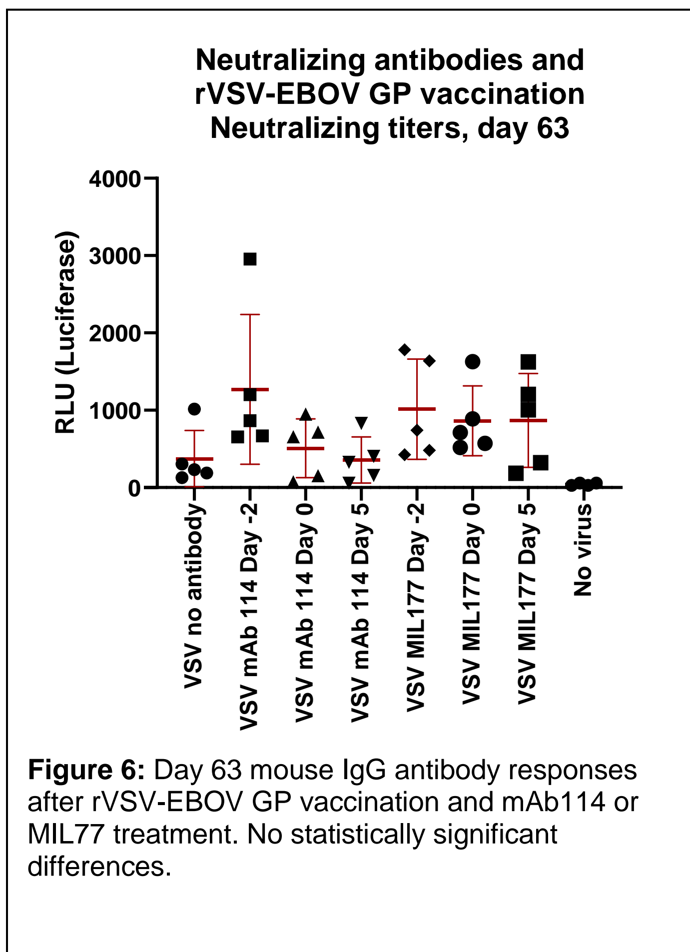

Figure 6: Day 63 mouse IgG antibody responses after rVSV-EBOV GP vaccination and mAb114 or MIL77 treatment. No statistically significant differences.

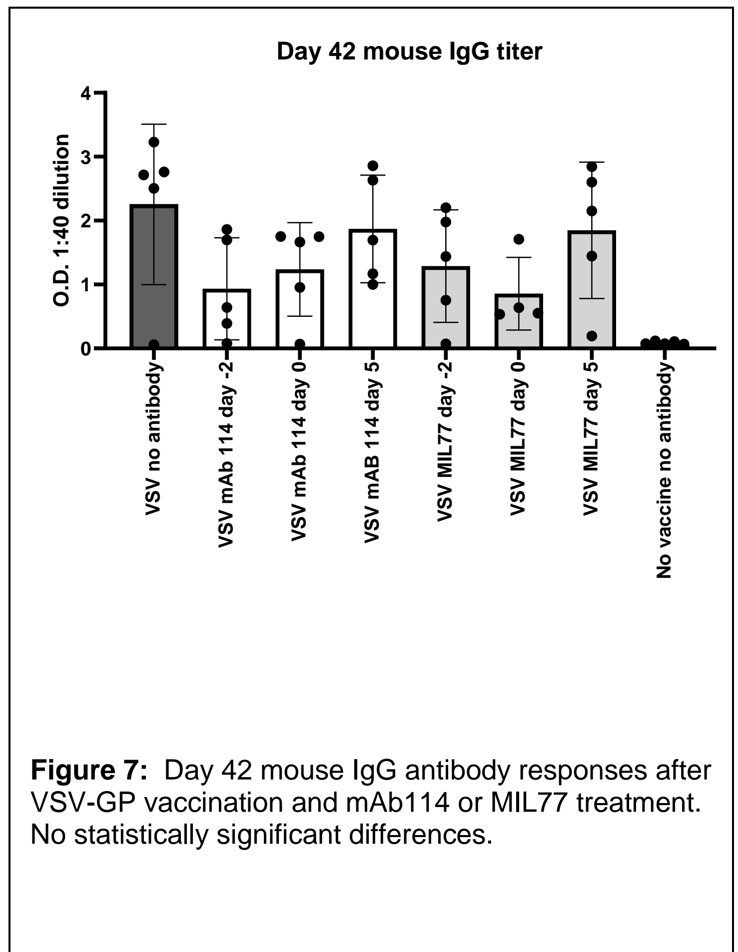

Figure 7: Day 42 mouse IgG antibody responses after VSV-GP vaccination and mAb114 or MIL77 treatment. No statistically significant differences.

Conclusions (both positive and negative)

1) In rVSV-EBOV GP vaccinated mice treated with remdesivir, there was an early increase in titers at day 5 in both the day -2 remdesivir treated, and the mock IV treated, compared to mice that did not receive IV injections until day 3 likely due to the effect of the IV injection itself rather than the remdesivir drug.

2) There were no significant differences in the titers of IgM/IgG in the remdesivir treated groups compared to the mock IV vaccine only group by day 21.

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- **d) other achievements**.

  - **Stated Goals not met.**

  - *Live virus challenge.* We were unable to conduct live Ebola virus challenge in our collaborators' BSL-4 facility due to this facility not being able to accommodate these requests because of the COVID-19 pandemic. We are hoping to conduct these experiments in the no-cost extension period as described in section 5.

  - *T cell analysis.* We have not yet conducted the day 63 T cell analysis. This work will be accomplished in the coming weeks. We have the splenocytes harvested and frozen for GP epitope responses.

- **What opportunities for training and professional development has the project provided?**

  - Student training: Elizabeth Clarke, Tonilynn Baranowski, Julianne Peabody, Sam Goodfellow, and Mahgol Behnia. This project has been used to fund the training of four PhD students and a postdoctoral fellow in the Bradfute laboratory. Dr. Clarke has

participated in the mouse injection, harvesting, and analysis aspects of the work as well as the antibody testing. Dr. Clarke obtained her PhD in January of 2021, and has stayed in the lab on a short-term postdoctoral fellowship. Dr. Clarke is still active in this project. Ms. Baranowski has helped set up the flow cytometric analysis for the T cell responses and is involved in the animal injection and handling aspects of the project. Ms. Behnia has been involved in mouse handling and tissue processing. Ms. Peabody and Mr. Goodfellow have assisted in injections, bleeds, and tissue processing. Together, this grant has significantly impacted the technical and scientific training of these four PhD students and one postdoctoral fellow.

- Research scientist training: Chunyan Ye and Robert Nofchissey. These two individuals are senior research scientists in the Bradfute laboratory with a long history of virus research. Ms. Ye is heavily involved in the injection, tissue processing, and antibody tests reported here. Mr. Nofchissey participated in the mouse injection and tissue harvesting, as well as in the overall setup and organization of the experiments.

- **How were the results disseminated to communities of interest?**
  - Nothing to report. This is due to the cancelation of multiple scientific meetings due to COVID-19 restrictions.

- **What do you plan to do during the next reporting period to accomplish the goals?**
  - We plan to complete the Year 3 goals that were not met in the no-cost extension period. This includes live virus challenge studies and T cell analysis that were postponed due to COVID-19 limitations or product acquisition issues.

- **IMPACT:**
  - **What was the impact on the development of the principal discipline(s) of the project?**
    - Nothing to report. We feel our findings will have an impact but additional experiments are being completed before peer review and publication.
  - **What was the impact on other disciplines?**
    - Nothing to report. We feel our findings will have an impact but additional experiments are being completed before peer review and publication.
  - **What was the impact on technology transfer?**
    - Nothing to report
  - **What was the impact on society beyond science and technology?**
    - Nothing to report

- **CHANGES/PROBLEMS:**
  - **Changes in approach and reasons for change**
    - We plan to substitute molnupiravir for favipiravir since the former drug has been shown to be effective in SARS-CoV-2 in humans and against EBOV in vitro, while favipiravir did not show efficacy in human trials conducted after the initial acceptance of this proposal. Remdesivir was kept in this study since initial studies suggest it may have a role as an inhibitor of persistent EBOV reservoir sites in human infection.
  - **Actual or anticipated problems or delays and actions or plans to resolve them**

- *COVID-19 and personnel limitations.* Due to COVID-19, our institution has limited operations capacity for much of 2020 and 2021. Staff capacity was set between 25-50% for most of that time. We have streamlined our large *in vivo* experiments by scheduling multiple personnel on bleed days, analyzing serum at one dilution measured against a monoclonal standard, and cross-training personnel for different kinds of injections. We have successfully completed much of the proposed work in Year 3 and hope to complete our pending Year 3 goals in the no-cost extension period.

- *COVID-19 and BSL-4 challenge studies.* Due to the SARS-CoV-2 pandemic, many experiments for this work were adversely affected. The planned BSL-4 live challenge experiments at NIH/NIAID/IRF were not able to be performed, as closures, personnel restrictions, and SARS-CoV-2 work took priority. Our plan to address this issue is to combine the Aim 1 live virus challenge studies (with vaccinated mice injected with monoclonal antibodies) alongside the live virus studies for Aim 2 as well as Aim 3 in the no-cost extension period. It is our hope the BSL-4 operations will be available for these studies during that time. Combining the three experiments will also reduce the number of mice to be used, since only one set of controls will be needed.

- *AdV-GP.* We did not conduct AdV-GP studies in Year 3, since a) we consistently saw significantly decreased antibody responses compared to VSV-GP vaccination and b) there is no foreseeable negative effects of antiviral drugs on a non-replicating vaccine. To reduce animal numbers we chose to continue with VSV-GP vaccination alone.

- *T cell analysis.* We have day 63 splenocytes frozen down from these experiments and will conduct the T cell assays in the no-cost extension year.

- **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**
  - No significant changes. A new IACUC protocol was approved from 2022-2025.

- **Significant changes in use or care of human subjects**
  - Not applicable

- **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

- **PRODUCTS:**

  - **Publications, conference papers, and presentations**

    - **Journal publications.** Dr. Bradfute has published an invited review entitled "Novel drug design strategies for filoviruses" (*Expert Opinion in Drug Discovery 2022 Feb;17(2):139-149. doi: 10.1080/17460441.2022.2013800, PMID: 34962451).* In it, he discusses the possibility of regimens with both antibodies and vaccines to provide short and long-term protection against EBOV. The manuscript lists this grant as support.

- A manuscript outline is being constructed based on our data, but we are waiting on the live virus challenges prior to submitting a manuscript.

- **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)**
  Nothing to report.

- **Technologies or techniques**
  Nothing to report.

- **Inventions, patent applications, and/or licenses**
  Nothing to report.

- **Other Products**
  Nothing to report.

- **PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS**

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

Name:	*Steven Bradfute*
Project Role:	*PI*
Researcher Identifier (e.g. ORCID ID):	0000-0002-1985-751X
Nearest person month worked:	4
Contribution to Project:	*Dr. Bradfute has overseen the project, including experimental design, acquisition of reagents, data analysis, and report generation.*
Funding Support:	*All of Dr. Bradfute's effort on this project came from this grant.*

Name:	*Elizabeth Clarke*
Project Role:	*Postdoctoral fellow*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*6*
Contribution to Project:	*Ms. Clarke has overseen the execution of the experiments and participated in injections, tissue harvesting, analysis of antibody levels, and generation of data.*
Funding Support:	*All of Ms. Clarke's efforts for this project have been funded by a T32 training grant.*

Name:	*Mahgol Behnia*
Project Role:	*Graduate Student*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	6
Contribution to Project:	*Ms. Behnia has been involved in animal handing, injections, and tissue processing.*
Funding Support:	*All of Ms. Behnia's efforts for this project have been funded by this grant.*

Name:	*Tonilynn Baranowski*
Project Role:	*Graduate Student*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*1*
Contribution to Project:	*Ms. Baranowski has been involved in animal handing, injections, and tissue processing.*
Funding Support:	*All of Ms. Baranowski's efforts for this project have been funded by this grant.*

Name:	*Julianne Peabody*
Project Role:	*Graduate Student*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*1*
Contribution to Project:	*Ms. Peabody has been involved in animal handing, injections, and tissue processing.*
Funding Support:	*Ms. Peabody's efforts are funded by a T32 training grant.*

Name:	*Samuel Goodfellow*
Project Role:	*Graduate Student*
Researcher Identifier (e.g. ORCID ID):	0000-0003-0471-8303
Nearest person month worked:	*1*

Contribution to Project:	*Mr. Goodfellow has been involved in animal handing, injections, and tissue processing.*
Funding Support:	*Ms. Peabody's efforts are funded by a T32 training grant.*

Name:	*Chunyan Ye*
Project Role:	*Research Scientist*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	9
Contribution to Project:	*Ms. Ye has been involved in animal handling, injections, tissue processing, antibody ELISAs, and neutralizing assays.*
Funding Support:	*All of Ms. Ye's efforts for this project have been funded by this grant.*

Name:	*Robert Nofchissey*
Project Role:	*Research Scientist*
Researcher Identifier (e.g. ORCID ID):	0000-0002-7368-6758
Nearest person month worked:	2
Contribution to Project:	*Mr. Nofchissey has been involved in animal handing, injections, and tissue processing.*
Funding Support:	*All of Mr. Nofchissey's efforts for this project have been funded by this grant.*

- **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:** United States Army Medical Research Institutes of Infectious Diseases (USAMRIID)
    - **Location of Organization:** Fort Detrick, MD, USA
    - **Partner's contribution to the projec**t
        - **Other.** USAMRIID (Dye lab) supplied the monoclonal antibodies used in the Year 1 and 2 reports
    - **Organization Name:** Rocky Mountain Labs, NIH/NIAID
    - **Location of Organization:** Hamilton, MT, USA

- **Partner's contribution to the project**

    - **Other.** RML (Feldmann lab) supplied the VSV-Ebola vaccine used in this Year 3 report

- **SPECIAL REPORTING REQUIREMENTS**

    - **COLLABORATIVE AWARDS:** Not applicable.

    - **QUAD CHARTS:** Not applicable.

- **APPENDICES:** Not applicable.