Attachment C-1

Covid-19 Grant Project Status Report

Before it will be possible to make any disbursement, you are required to provide to the Agency the status towards the specific purpose as stated in the grant contract (Attachment A-1). This report is to be completed by the grant recipient and each subrecipient. The grant recipient is to ensure all subrecipients' reports are to be included with cost reimbursement requests. RECIPIENT COMPLETION INFORMATION:

Upload forms using the following link: https://ncosbm.sharefile.com/r-rc7f2ca49d574af2a

1. Organization

Organization Name	North Carolina Policy Collaboratory at the University of North Carolina at Chapel Hill (GSPH/Epidemiology/Baric H5L02)
Contract Agreement Number	23-01
Date	February 15, 2021

2. Financial Summary

Total Funding Authorized	Total Funding Received to Date	Balance
460,505	$465,319.91	$4,814.91 overdrawn. Additional funds used are from the balance remaining on H5L03 (Bowman)

Collaboratory Covid-19 Research Summaries

COVID-19 NC Collaboratory Projects: Antiviral Accelerator

Start of Block: Contact Information

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Department of Epidemiology

Q5 Primary Institution

- O Appalachian State University (1)
- O Elizabeth City State University (2)
- O Fayetteville State University (3)
- O NC A&T University (4)
- O NC Central University (5)
- O NC State University (13)
- O UNC Asheville (6)
- O XX UNC Chapel Hill (7)
- O UNC Charlotte (8)
- O UNC Greensboro (9)
- O UNC Pembroke (10)
- O UNC Wilmington (14)
- O Western Carolina University (11)
- O Winston Salem State University (12)

Start of Block: Research Project Information

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Q6 Succinctly state your research question in 2-3 sentences (character limit 100).

The goal is to produce 1st generation SARS-CoV2 coronavirus vaccines for testing in robust mouse models of human disease, providing critical data for downstream collaborations with academic, federal, and commercial partners. Development of broad spectra (cross-protective) group 2b Sarbecovirus and group 2c Merbecovirus vaccines and begin to test these vaccines in robust mouse models of human disease, providing critical data for downstream collaborations with academic, federal, and commercial partners.

Q7 **Describe your research methods and activities in a short paragraph. Please use plain language and avoid technical terms unless necessary. (character limit 1,000).**

We isolated spike genes from a variety of coronaviruses and inserted these spike glycoprotein genes into virus vaccine vectors based on alphaviruses, engineered to express foreign vaccine immunogens in a safe and effective manner. After validating that the genes expressed authentic coronavirus spike glycoproteins, we will vaccinate mice and measure immune responses afterward. Then the mice will be challenged with SARS-CoV-2 and then other related clade I and IIII coronaviruses, evaluating the breadth of protection across different SARS-like coronaviruses. We will also build alphavirus vectors that express different S glycoproteins from the contemporary human coronavirus as well as other group I and group II emerging coronaviruses which threaten human populations. After vaccination of mice, we will determine the ability of these vaccine candidates to protect against SARS-CoV2 and other related CoV.

Q8 **Describe your research findings and conclusions in a short paragraph. Please use plain language and avoid technical terms unless necessary. (character limit 1,000)**.

After vaccination, neutralization assays revealed strongly neutralizing activity in the serum from mice at 3 weeks post vaccination with the SARS-CoV2 spike, but not nucleocapsid or GFP proteins. Only animals vaccinated with SARS-CoV-2 spike expressing vaccines exhibited protection from infection as demonstrated by no changes in body weight, protection from severe disease, and total elimination of viral titers in the lungs. Interestingly, viral titers were still detectable on 2 and 4dpi after infection in nasal turbinate tissue suggesting that sterilizing mucosal immunity in the nasal passages may be difficult to achieve. We also evaluated the ability of related SARS-like S glycoprotein vaccines to protect from heterologous SARS-CoV2 challenge. We saw protection from weight loss and mortality, but not virus replication suggesting that broad based vaccines are possible, but that additional modifications are needed to maximize universal vaccine performance. We did not see any protective immunity using contemporary human coronaviruses or MERS-like viruses from SARS-CoV2 challenge, suggesting that additional modifications are needed to generate a uiversal CoV vaccine.

Q9 From your perspective as a researcher, explain any implications or policy recommendations resulting from your research (character limit 1,000).

Our data clearly support the idea that efficacious SARS-CoV2 vaccines can be achieved for human populations. Our data also support the hypothesis that broad based group 2b SARS-like vaccines can be achieved with additional research. Our data argue that more comprehensive universal coronavirus vaccines will be difficult to achieve, but possible, using multiplexing strategies that encode multiple group 1 and group 2 coronavirus immunogens either in complex as a single vaccine strategy or via the use of chimeric immunogens that capture key neutralizing epitopes from multiple heterologous group 2 coronaviruses. We recommend that the research community continue to focus research on universal vaccine development, as such vaccines are critical to prevent future pandemic coronaviruses.

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End of Block: Research Project Information

Start of Block: By the Numbers

Q11 How many members were a part of your research team? Include faculty, staff, postdoctoral researchers, graduate, and undergraduate students. If a type does not apply, please indicate with a numeric zero (0).

O Faculty (1) Lisa Gralinski

O Staff, permanent (7) Vaughters, Baric, Scobey, Brewer-Jensen, Mallory, Munt, and Parrish

O Staff, temporary (0) _____

O Postdoctoral researchers (0) _____

O Graduate students (0) _____

O Undergraduate students (0)_____

Q12 How many community members or participants did you engage in your research project? If not applicable, please indicate with a numeric zero (0).

_____Two Faculty at UNC_____

Q20 How many University-external stakeholders or partners did you work with as part of your research project? If not applicable, please indicate with a numeric zero (0).

One Faculty Member at Duke University, One Faculty member at University of Washington

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Q18 Please detail any other interesting project-specific metrics (e.g. number of samples) that are relevant to your project below.

We were co-investigators on a NIH PO1 grant submitted from Duke University in collaboration with Bart Haynes. Although our project was well received, the overall program did not receive a funded score. We are resubmitting this application in Jan 2021. In another milestone, we are collaborating with Carbon Inc (https://carbon3d.com/) and Joseph DeSimone on SARS2 vaccines and have submitted a grant developing micro-delivery patches to introduce VRP-S and related vaccines into the skin. The grant was submitted in Oct 2020 and the reviews should become available in early March 2021.

Papers: Walls AC, et al., . Elicitation of Potent Neutralizing Antibody Responses by Designed Protein Nanoparticle Vaccines for SARS-CoV-2. Cell. 2020 Oct 31:S0092-8674(20)31450-1. doi: 10.1016/j.cell.2020.10.043. PMID: 33160446; PMCID: PMC7604136.

Leist SR, Dinnon KH 3rd, et al. A Mouse-Adapted SARS-CoV-2 Induces Acute Lung Injury and Mortality in Standard Laboratory Mice. Cell. 2020 Sep 23:S0092-8674(20)31247-2. PMCID: PMC7510428

Q13 Were you able to leverage additional funding to continue the research funded by the NC General Assembly through the NC Policy Collaboratory?

O Yes (1)

OX No (2)

Display This Question:

If Were you able to leverage additional funding to continue the research funded by the NC General As... Yes

Q15 Please detail the amount of leveraged funding and the funding agency or agencies below. If you received funding from more than 5 sources, please email Hope Thomson at thomson1@email.unc.edu .

	Funding Amount ($) (1)	Funding Agency (2)
Funding Source 1 (1)		
Funding Source 2 (2)		
Funding Source 3 (3)		
Funding Source 4 (4)		
Funding Source 5 (5)		

Q16 Do you have a grant in progress or plan to apply for additional funds to continue your work as funded by the Collaboratory? If so, please detail the grant amounts and funding agencies below to the best of your knowledge.

DeSimmone, Baric NIH; 6/2021-2026 Baric UNC Chapel Hill total Budget: $ 1,783,140
Haynes, Baric NIH; NIH PO1 6/2021-2026 Baric UNC Chapel Hill Budget $ 3,750,000

Q17 Please include below any links to news coverage, press releases, or other public-facing documentation of your Collaboratory-funded work:

None

End of Block: By the Numbers