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 H5L01)
Contract Agreement Number	23-01
Date	February 15, 2021

2. Financial Summary

Total Funding Authorized	Total Funding Received to Date	Balance
1,592,929	1,639,103.65	$46,174.65 overdrawn. Additional funds used are from the balances remaining on Baric H5L09, Bowman H5L03, Westreich H5L04, Gordon-Larsen H5L05, and Powers H5L06.

Collaboratory Covid-19 Research Summaries

COVID-19 NC Collaboratory Projects: High-throughput equipment grant Baric, R

The goal is to establish high-througput platforms to rapidly test and evaluate biotech products and vaccine performance using in vitro neutralization and drug assays for ..... . To achieve these goals, we will purchase equipment for BSL3 facilities on UNC Campus to promote high-throughput analyses of samples from COVID 19 patients and from

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Start of Block: Contact Information

Ralph S. Baric, PhD
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Chapel Hill, NC 27599-7435

Q2 Email Address

rbaric@email.unc.edu

Q3 Department

Department of Epidemiology

Q5 Primary Institution

XXO UNC Chapel Hill (7)

End of Block: Contact Information

Start of Block: Research Project Information

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

The goal of this program is to establish BSL2 and BSL3 high-throughput platforms to rapidly test and evaluate biotech products and vaccine performance using in vitro neutralization and drug assays for SARS-CoV. To achieve these goals, we will purchase equipment for BSL3 facilities on UNC Campus to promote high-throughput analyses of samples from COVID 19 patients and for high-throughput drug analyses, as well as translational research. We will also use these facilities to characterize antibody responses after infection or vaccination and against new variants as they arise in human populations.

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 have purchased and installed all equipment, hired and trained staff members, and have begun research in our fully operational BSL3 facility for high-throughput research. Staff have been trained in high-throughput equipment use and we have begun implementing these equipment items into protocols for conducting high throughput assays. Importantly, we have published manuscripts and leveraged these dollars to obtain significant research support for downstream studies.

We have evaluated several large blocks of antibodies for their capacity to neutralize and protect mice from lethal SARS-CoV2 infection, working closely with several investigators throughout the United States and identified several highly potent cross neutralizing antibodies that target multiple Sarbecoviruses. Using these antibodies in combination with a small molecule nucleoside inhibitor, we show that the combination therapy is much more efficient at extending the therapeutic window, while improving outcomes both under prophylactic and therapeutic conditions. Finally, we have also developed a new mouse model to evaluate therapeutic drugs that block SARS-CoV2 and related SARS-like coronaviruses in vivo.

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).

We have developed state of the art facilities that are equipped to allow for high throughput evaluations of natural infection and vaccine serum samples and drugs that neutralize or inhibit SARS-CoV2 replication in vitro and replication and pathogenesis in vivo. These facilities include high-throughput capabilities that can be used at both in the BSL2 and BSL3 laboratory. We have used these facilities to evaluate the neutralization titers of serum samples from vaccinee's and from natural infection groups, and to identify the neutralization potency of human monoclonal antibodies derived from COVID19 patients. We have then evaluated these antibodies for their ability to neutralize SARS-CoV2 infection both in vivo and in vitro, while also developing new mouse models for evaluating the pathogenic potential of emerging coronaviruses and the ability to inhibit virus replication in vivo.

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

The development of these facilities allowed us to successfully compete for OWS funding to evaluate vaccine performance in humans, helping to move the Moderna COVID19 mRNA vaccine forward toward emergency use authorization for use in human populations.

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 (0) _____
- O Staff, permanent (1) Kalyn Parrish
- O Staff, temporary (0) _____
- O Postdoctoral researchers (3) Moreira, Meganck, and Hou
- 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).**
Five: Boucher, Dittmer, Damania, Randall, Miller

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).
Seven, Kawaoka, Halfman, Chiba, Ravetch, Bieniasz, Bowen, Nussenzweig, Graham, Beigel

* Q**18 Please detail any other interesting project-specific metrics (e.g. number of samples) that are relevant to your project below**
Wahl A, Gralinski LE, Johnson CE, Yao W, Kovarova M, Dinnon KH 3rd, Liu H, Madden VJ, Krzystek HM, De C, White KK, Gully K, Schäfer A, Zaman T, Leist SR, Grant PO, Bluemling GR, Kolykhalov AA, Natchus MG, Askin FB, Painter G, Browne EP, Jones CD, Pickles RJ, Baric RS, Garcia JV. SARS-CoV-2 infection is effectively treated and prevented by EIDD-2801. Nature. 2021 Feb 9. doi: 10.1038/s41586-021-03312-w. PMID: 33561864

Anderson EJ, Rouphael NG, Widge AT, Jackson LA, Roberts PC, Makhene M, Chappell JD, Denison MR, Stevens LJ, Pruijssers AJ, McDermott AB, Flach B, Lin BC, Doria-Rose NA, O'Dell S, Schmidt SD, Corbett KS, Swanson PA 2nd, Padilla M, Neuzil KM, Bennett H, Leav B, Makowski M, Albert J, Cross K, Edara VV, Floyd K, Suthar MS, Martinez DR, Baric R, Buchanan W, Luke CJ, Phadke VK, Rostad CA, Ledgerwood JE, Graham BS, Beigel JH; mRNA-1273 Study Group. Safety and Immunogenicity of SARS-CoV-2 mRNA-1273 Vaccine in Older Adults.N Engl J Med. 2020 Dec 17;383(25):2427-2438. doi: 10.1056/NEJMoa2028436. PMID: 32991794

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

McNamara RP, Caro-Vegas C, Landis JT, Moorad R, Pluta LJ, Eason AB, Thompson C, Bailey A, Villamor FCS, Lange PT, Wong JP, Seltzer T, Seltzer J, Zhou Y, Vahrson W, Juarez A, Meyo JO, Calabre T, Broussard G, Rivera-Soto R, Chappell DL, Baric RS, Damania B, Miller MB, Dittmer DP. High-Density Amplicon Sequencing Identifies Community Spread and Ongoing Evolution of SARS-CoV-2 in the Southern United States. Cell Rep. 2020 Nov 3;33(5):108352. doi: 10.1016/j.celrep.2020.108352.

Hou YJ, Chiba S, Halfmann P, Ehre C, Kuroda M, Dinnon KH, Leist SR, Schäfer A, Nakajima N, Takahashi K, Lee RE, Mascenik TM, Edwards CE, Tse LV, Boucher RC, Randell SH, Suzuki T, Gralinski LE, Kawaoka Y, Baric RS. 2020. SARS-CoV-2 D614G Variant Exhibits Enhanced Replication ex vivo and Earlier Transmission in vivo. Science. 2020 Nov 12:eabe8499. doi: 10.1126/science.abe8499. Online ahead of print. PMID: 33184236.

Schäfer A, Muecksch F, Lorenzi JCC, Leist SR, Cipolla M, Bournazos S, Schmidt F, Maison RM, Gazumyan A, Martinez DR, Baric RS, Robbiani DF, Hatziioannou T, Ravetch JV, Bieniasz PD, Bowen RA, Nussenzweig MC, Sheahan TP. Antibody potency, effector function, and combinations in protection and therapy for SARS-CoV-2 infection in vivo. J Exp Med. 2021 Mar 1;218(3):e20201993. doi: 10.1084/jem.20201993. PMID: 33211088; PMCID: PMC7673958

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

X Yes

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.

1. Proposal Number: No. 20-0943:
Title: “WARP Speed Assay development” Baric, R (PI) Batelle
9/1/2020-7/1/2021 Direct Costs: $682,384
The subcontractor will complete assay optimization, qualification, validation, preparation for scale-up and tech transfer for the Neutralization Assay to quantify neutralizing antibodies to SARS-CoV-2 in human sera by no later than the end of 12/20. The subcontractor will provide a tech transfer package, reagents necessary to complete transfer of the assay, final qualification and validation protocols and reports, and a comparability testing protocol and report.

2. NIH AID AI149644-02S1 Respiratory Virus Vaccine and Adjuvant Exploration
- Equipment Supplement. Baric R (PI) NIH AID
09/04/2020 – 03/31/2021 Direct Costs: $1,088,512
To help build UNC’s infrastructure to support COVID19 research and clinical studies, we used state CCP support to request additional funds from the National Institute of Health to equip additional BSL3 space with equipment that will support COVID19 research. The supplement was funded.

Q15 Please detail the amount of leveraged funding and the funding agency or agencies below. continued....

3. NIH3 UM1AI068618-14S2: Baric, R PI NIH AID
CoVPN 3002. A Phase III Randomized, Double-blind, Placebo-controlled Multicenter Study in Adults to Determine the Safety, Efficacy, and Immunogenicity of AZD1222 for the Prevention of COVID-19 LAB. Phase I: $740,391.00

4. NIH AID3 UM1AI068618-14S1-REVISED: Baric, R PI NIH AID
CoVPN 3001 A Phase 3, Randomized, Stratified, Observer-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine in Adults Aged 18 Years and Older. Phase I: $2,931,804.00

5. NIH NCI U54CA260543; Oct 1, 2020-Sept 31, 2022; NIH NCI
Baric, RS PI, North Carolina Seronet Center for Excellence. $3,974,612;
with opportunity for three additional years of funding if successful metrics are achieved through year 2.

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.

No

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