Appendix II

Budget Allocation

Personnel Costs: $116,355
Fringe: $ 38,494

Non-personnel Costs: $310,656

Total: $465,505

**Per UNC CH Policy, personnel fringe will be paid by the Collaboratory from this award prior to funding transfer.*

Budget Summary

EHRA Salary	$ 36,667
SHRA Salary	$ 79,688
Grad Student	$0
Temps	$0
Fringe Pool	$ 38,494
Non-Personnel Expenses	$310,656
Total	**$465,505**

Appendix III

BARIC Project 1. Basic-Emerging CoV Vaccine Development: Development of broad spectra (cross-protective) group 2b Sarbecovirus and group 2c Merbecovirus vaccines. The goal is to produce 1st generation vaccines for testing in robust mouse models of human disease, providing critical data for downstream collaborations with academic, federal, and commercial partners. Team includes: Baric, Sheahan, Moorman, Heise.

Impact to the State (300 word limit)

- Description of the problem or challenge being addressed and how the problem impacts those in the state of North Carolina
- Describe how the proposed research will provide impactful solutions to the described problem to help the state of North Carolina

Zoonotic coronaviruses are responsible for three major epidemics/pandemics in the 21st century, including Severe Acute Respiratory Coronavirus (SARS-CoV) in 2003 and Middle East Respiratory coronavirus (MERS-CoV) in 2012. In late 2019, SARS-CoV-2 emerged in Wuhan China and in the space of 5 months, has caused over 3.5 million cases, >250,000 deaths in >200 countries. Over 1/3 of these total cases have been reported in the US, resulting in over 72,000 deaths.

Using complementary expertise in viral immunity, coronavirus pathogenesis, antibody repertoire mapping, vaccinology and structure-based vaccine design, we will develop an integrated program to develop pan-betacoronavirus vaccines that protect against the Merbecoviruses (MERS-like group 2c) and Sarbecoviruses (SARS-like group 2b CoV).

The impact is that we will use our unique mouse models of human disease, using hACE2-or hDPP4 transgenic mice and more importantly, the first mouse adapted SARS-CoV-2 variant that replicates efficiently and produces ARDS like disease phenotypes in standard laboratory mice, as well as several adapted SARS-CoV strains and reporter viruses that provide precise measures of neutralizing antibody titer, breadth and magnitude following natural infection and vaccination. We note that mouse models of human disease exist for all of these heterogenous strains, allowing us to access vaccine breadth upon lethal homologous and heterologous challenge. Using these models, the goal is to produce 1st generation vaccines for testing in robust mouse models of human disease, providing critical data for downstream collaborations with academic, federal, and commercial partners.

Milestones (300 word limit):

Description of what will be accomplished and what can be delivered by August 31, 2020, and by Dec. 31, 2020. The start date will be June 1, 2020.

<u>August 31,2020 Milestones</u>

- Construct and validate SARS-CoV-2 and related clade III group 2b S glycoprotein expression from alphavirus VRP 3526 Expression Vectors
- Immunize mice with SARS-CoV-2 and related clade IIII S glycoprotein VRP vectors

Dec, 31, 2020 Milestones

- Measure serologic and neutralization responses in VRP vaccinated mice
- Challenge mice with SARS-CoV-2 and related clade III group 2b coronaviruses
- Demonstrate protective immunity

Budget Justification (200 word limit): Funds are limited. We encourage all teams to revisit their budget and determine if it can be reduced.

4 month salary support for Research Assistant Professor

Funds are requested to support the salary of 7 laboratory staff members for a total of 27.5 calendar months (average of 4 months per staff member). 0.24 calendar months are also requested to support an accounting technician.

Fringe Benefits
Benefits are for faculty and staff as follows: Faculty and Staff – 25.889% Social Security and retirement and $6,512.00 for health insurance

Supplies
Supplies critical to the completion of this project include cell culture, synthetic DNA, PPE, serum, Media, plasticware, RNAseq, chemicals, disinfectants, Animals, flow cytometry, kits, antibodies, enzymes, Cytokine measurements by bioplex, pipettes, nLUC assays, liquid handler disposables, etc.

Other Expenses
Funds are requested for maintenance costs of laboratory equipment essential to the completion of this projects. Requested funds are proportional to the anticipated use of the equipment for this project.