FUNDING OF PROGRAMS TO PROVIDE AID TO NORTH CAROLINIANS IN RESPONSE TO THE COVID-19 CRISIS AT THE BRODY SCHOOL OF MEDICINE

August 31, 2020
As required by Session Law 2020-4, Section 24

ECU BRODY SCHOOL OF MEDICINE

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I. Introduction

In Session Law 2020-4, "An Act to Provide Aid to North Carolinians in Response to the Coronavirus Disease 2019 (COVID-19) Crisis," the North Carolina General Assembly provided support to the Brody School of Medicine at East Carolina University for its efforts to advance care for the people of North Carolina, specifically stating (S.L. 2020-4 §24):

> $15,000,000 to the Brody School of Medicine at East Carolina University to be used for (i) the rapid development of a countermeasure of neutralizing antibodies for COVID-19 that can be used as soon as possible to both prevent infection, and for those infected, treat infection, (ii) bringing a safe and effective COVID-19 vaccine to the public as soon as possible, (iii) community testing initiatives, and (iv) other research and activities related to COVID-19. By September 1, 2020, the Brody School of Medicine shall submit a report on the progress of the development of a countermeasure and vaccine, findings from their community testing initiatives, and other research and activities related to COVID-19, and the use of the appropriated funds received pursuant to this subdivision to the Joint Legislative Oversight Committee on Health and Human Services.

The mission of the Brody School of Medicine is to increase the supply of primary care physicians serving the state, to improve the health status of eastern North Carolina's citizens, and to enhance access of minority and disadvantaged students to a medical education. The COVID-19 crisis represents a challenge in each of these areas, and the General Assembly's mandate to the school supports activities that are entirely within the Brody mission: each of the four priorities are enhancing our ability to safeguard our campus, manage the health of individuals in our community suffering from the pandemic, and serve the health of minority and disadvantaged communities while encouraging young people to pursue a career in health sciences.

As required under the law, this report represents the first report on progress to date achieved by the Brody School of Medicine to combat COVID-19 and to understand and protect the community we serve from the virus SARS-CoV-2.

II. Summary Narrative

The Brody School of Medicine has approached the challenge of COVID-19 while staying true to the school's mission, which remains unchanged from the founding vision in 1974. Fidelity to this mission and vision has resulted in a school whose focus is the members of our community who have historically failed to benefit from healthcare. ECU houses the North Carolina Agromedicine Institute, which focuses on farm workers, foresters, and fishermen who serve the state's agricultural economy. Brody's greatest contributions have focused on the health conditions endemic in our community, from obesity and diabetes to heart disease.

While initial outbreaks were in cities, drawing international attention to Wuhan in Hubei Province, China, Milan, Italy, Seattle, Washington, and New York, New York, over time the virus has diffused more broadly across the country. The national story of COVID-19 has been one of tension and relief, tension and relief, however for the majority of the country the case rates have increased monotonically (Figure 1). The lack of correlation between national hotspots and regional case rates has enhanced the importance of regional efforts. The Brody School of Medicine has endeavored to serve as a center of community support for our region.

This has manifested first in our clinical work. The Brody School of Medicine's Pathology Department under Chair John Fallon has overseen a massive testing initiative. Through August 27, the Pathology Department, working with ECU-Physicians and Vidant Health, have evaluated over 90,000 RT-PCR tests for the SARS-CoV-2 virus, and over 4,000 serology tests for virus antibodies. They have also overseen deployment of the new antigen test, a point-of-care test that generates results in 15 minutes for patients in clinics. Dr. Fallon has rapidly built capacity in the hospital lab, with support from Vidant Health. This has allowed Vidant to evaluate nearly 3,500 tests in rural testing events with results returned within 24 hours. The lab has also conducted over 5,500 tests on behalf of the Pitt County Health Department. The Brody Department of Family Medicine was one of the first drive-through testing sites in the state, offering sample collection behind the Medical School's premier family medicine center.

For Brody's Department of Internal Medicine, home to the school's experts in infectious diseases and critical care, the pandemic has mobilized an impressive array of initiatives. From serving as a leading site for clinical trials to serving as an innovator in outreach to underserved communities, the Department of Internal Medicine provides the heart of ECU's response to COVID-19. For many research studies, Brody's Department of Internal Medicine has been a leading site nationally for participant recruitment, from the studies of convalescent plasma recently in the news to clinical trials of novel antibodies. Participant recruitment has been extended across the Vidant Health network, enabling Brody trial leaders to recruit participants

from diverse demographics. This diversity is sorely needed as COVID-19 has had a terrible impact on populations often medically underserved across the state and the nation.

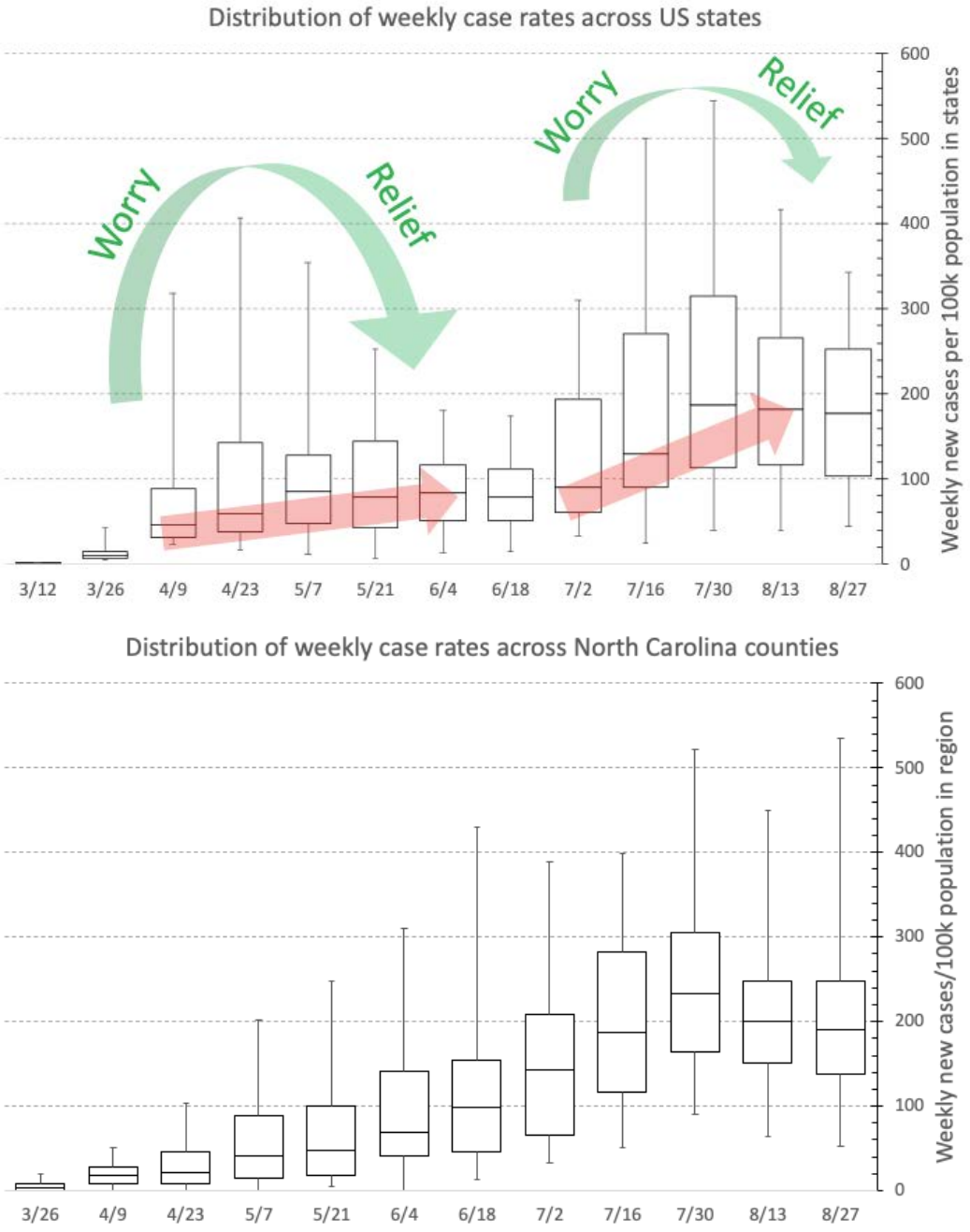

Figure 1: The range of per capita weekly new case rates in US states (above) and North Carolina counties (below) shown in boxplots as cases per 100,000 population over time. While the perception of COVID-19 in the US has focused on the history of case rate growth and contraction in US hotspots (green arrows; e.g., Seattle, New York, Florida), the impact of the disease in North Carolina has broadly followed the national median (red arrows).

With eastern North Carolina's diverse communities comes diverse exposures, and the Brody mission has enabled the school to assemble a strong team of microbiologists with experience researching exposure-related pathology. Brody entered the pandemic with one of the leading experts from the first SARS epidemic, Dr. Rachel Roper, and Dr. Mark Mannie, whose expertise is in mechanisms involved in the phenomenon of the "cytokine storm" with funding from Dr. Anthony Fauci's NIAID. These and other scientists have expanded their efforts to address the ongoing pandemic.

As the COVID-19 pandemic evolves from an outbreak to an endemic disease in communities, our focus on it also evolves from an urgent need for biological insight to a drive to understand the ways it is impacting communities. When two cases of Ebola were present in the United States, their management was trusted to the expert insight of world leaders in the management of emerging infectious disease. With more than 165,000 cases in North Carolina alone, COVID-19 needs to be managed based on evidence and in communities. COVID-19 so far this year has three times the incidence of diabetes in a typical year, and it disproportionately is impacting medically underserved communities. COVID-19 is a threat directly aligned with mission of the Brody School of Medicine.

III. Detailed Status Report

The mission of the Brody School of Medicine has influenced every project supported by S.L. 2020-4 funding. Projects were selected based on the guidance provided by the legislature as seen through the lens of the Brody mission. The projects described below represent the contributions of diverse stakeholders from across the Brody community and drawing on expertise from across the campus, with support targeted to project leaders who have demonstrated energy and enthusiasm in their efforts.

There is no clinically proven antiviral treatment regimen for SARS-CoV-2/COVID-19 and most clinical approaches used to care for patients suffering from the disease remain best classified as experimental. Progress has been hampered in our region particularly by the detrimental impact underlying patient comorbidities have on SARS-CoV-2 infectivity and pathogenesis. While the nuances of SARS-CoV-2 infection remain unclear, scientists have already identified many mechanisms for its transmission, uptake into a human host, pathological mechanisms, and the clinical course of infection. Many of the identified mechanisms are directly linked to underlying health conditions with high incidence in eastern North Carolina, and therefore align with expertise already at the Brody School of Medicine. In many cases, noted below, existing research at Brody represents a strong foundation to jumpstart research into COVID-19.

Outlined below is the full array of projects the Brody School of Medicine has initiated to fight the COVID-19 pandemic. Among these can be found:

- **Clinical research,** focused on rapidly deployable techniques to improve patient outcomes based on science we know;

- **Translational research,** where Brody scientists are bringing new developments from bench to bedside;
- **Basic science,** where Brody's and ECU's scientists have identified a novel insight that, if quickly pursued, could deliver a benefit to patients infected with SARS-CoV-2 today or in the near future; and
- **Public health research,** drawing on Brody's rural-focused public health faculty to understand the impact of COVID-19 on our region and applying new and time-tested public health approaches to provide relief to North Carolinians.

The goal is to rapidly provide relief, slow progression, and contribute to progress aimed at slowing or halting disease progression, preventing long-term sequelae, and providing a more tolerable antiviral treatment regimen for patients with complicating comorbidities.

All projects will incorporate graduate and professional students to better advance the aim of training the future workforce to be ready for the next crisis.

Strategy One: Enhancing Innate Immunity

Item: "(i) the rapid development of a countermeasure of neutralizing antibodies for COVID-19 that can be used as soon as possible to both prevent infection, and for those infected, treat infection…"

1. Building insight from convalescent plasma

The recent Food and Drug Administration (FDA) emergency use authorization (EUA) for convalescent plasma represents a concrete step in the development of "neutralizing antibodies for COVID-19" and represent the first step in the progression on this pathway. The effective treatment of a viral infection is accomplished by providing enhancements to innate mechanisms. The vision for developing such a treatment for COVID-19 starts with the evaluation of how each recovered person's innate immunity fought the virus, which we do through the transfusion of plasma from recovered individuals.

As scientists evaluate the biological factors that contribute to the success of plasma treatment, this leads to identification of specific molecular components of therapeutic value. This can prime the drug development pipeline, resulting the identification of disease-modifying targeted therapeutics that can be mass-produced by a pharmaceutical company and proven in trials overseen by academic experts who will guide the treatment through trials for safety, dosing, and efficacy.

ECU and the Brody School of Medicine have been significant contributors in this effort since the earliest days of the pandemic as a participating site in the Mayo Clinic's national research initiative that provided the data supporting the FDA's EUA. With the first subjects recruited into the study in April, four by the first day after regulatory approval of participation, Brody faculty recruited 137 subjects into this study. The Brody School of Medicine supported this

effort with its own funds initially and has utilized funds from S.L. 2020-4 to support the continuation of this initiative under the leadership of Dr. Paul Bolin, Chair of Brody's Department of Internal Medicine and Dr. Paul Cook, Chief of the Division of Infectious Diseases.

Initially offered at Vidant Medical Center, Dr. Bolin quickly expanded the program to support recruitment at 4 regional hospitals and the 137 participants have been enrolled from across the region. Focusing on the potential insight for future therapy, the study team has stored plasma from participants drawn before and after the plasma infusion to support reverse translation: the study of the mechanisms underlying care outcomes. Given the complexity of the human immune response, often it is this approach that provides the greatest insight, and, in the case of COVID-19, this has led to further studies.

As of the date of this report, much of the research effort is transitioning to clinical trials of therapeutic agents informed from these efforts. Brody's Department of Medicine has initiated over a dozen funded clinical trials, sponsored by industry partners and seeking to advance COVID-19 therapeutic agents. The research team is also contributing to diverse natural history studies, to advance our understanding of the diverse outcomes of innate immunity, including in individuals with underlying health conditions and across demographics. In many of these trials, the Brody team is among the national leaders in enrollment and in one we are the largest center in the country. In contrast to many other centers, the inclusion of Hispanic and African American populations in these studies match or are near the percentage infected in the population.

Thanks to the diverse population in eastern North Carolina, ECU is in a unique position to conduct reverse translation studies, and using funds provided by S.L. 2020-4, Brody's Department of Internal Medicine has started to evaluate how the chain of biochemical reactions that combine to form the body's immune response differ across our community, and to link those differences to patient outcomes. Brody scientists are currently evaluating the protein content of blood plasma before and after treatment in our clinical trials to look for direct and indirect markers of immune system function, to better validate investigational treatments and to elucidate mechanisms for treatments. This work is ongoing but has tremendous potential to facilitate management of COVID-19 and emerging diseases in the future. One promising study, supported by S.L. 2020-4 is being conducted by the Division of Hematology and Oncology's Dr. Li Yang, a biologist who specializes in vascular biology and inflammation – a critical intersection in COVID-19.

2. Modulating immune response with GPR4 inhibition

Dr. Yang is studying the role of a transmembrane receptor identified as GPR4, one of the class of G protein-coupled receptors first identified for its role in the sensing of the acidity of blood. Dr. Yang has studied this and related mechanisms and has published extensively on GPR4. He has compiled evidence that this receptor may be important in modulating the immune

response and could play a part in addressing the risk of acute respiratory distress syndrome (ARDS).

ARDS is a major cause of mortality and morbidity in individuals with COVID-19. In response to infection with SARS-CoV-2, ARDS develops when components of cellular immunity, inflammatory leukocytes, infiltrate into lung tissues. This is associated with diffuse alveolar damage, increased blood vessel leakiness, and lung edema that can lead to the well-known reduction in blood oxygen saturation (hypoxemia), respiratory failure and death. The goal of this research project is to study the role of GPR4 in modulating the inflammatory response in COVID-19 and to evaluate targeted GPR4 antagonists as potential therapeutics to stop the dangerous cascade of immune responses in infected individuals.

Working in the newly renovated Biosafety Level 3 laboratory (BSL3; addressed below), Dr. Yang and his team will develop and evaluate the effects of GPR4 small molecule inhibitors (provided by Novartis through collaboration) and therapeutic antibodies in preclinical animal models related to COVID-19. The team has secured a partnership with Novartis and has an animal use protocol approved by the Institutional Animal Care and Use Committee (IACUC) to conduct SARS-CoV-2 research in transgenic mice expressing the human ACE2 receptor and the mice are being produced. A colony will be established at ECU to support ongoing research. A second protocol has been approved by the IACUC for a mouse model of ARDS. This model does not require BSL3-level precautions and will research with this model has started as of the date of this report.

In parallel with these mechanistic studies, animal models based on GPR4 monoclonal antibodies (i.e., antibodies identified in patients and produced by cloned immune system cells) will be evaluated. Optimized antibody therapy is a powerful potential targeted intervention.

The very promising potential of the GPR4 interaction offers an opportunity to treat ARDS associated with COVID-19. There are diverse mechanisms at play in the human disease and understanding them will help with management of active SARS-CoV-2 infection, its sequelae, and inform our approaches to future emergent diseases.

3. Mapping the chemistry of SARS-CoV-2 proteins

With support from S.L. 2020-4, the Brody School of Medicine's Department of Biochemistry will focus on characterizing and disrupting virus-host protein-protein interactions for three different molecular targets, identified from over 300 host-viral protein-protein interactions in SARS-CoV-2 for their therapeutic potential. Each of these targets is positioned at a key regulatory step in the virus's lifecycle and is important to infectivity and pathogenesis. These three targets represent critical components of the pathogenic pathway as they are linked to viral entry into the cell, virus-mediated immune suppression, and viral replication in the host cell. These protein-protein interactions are involved in infectious mechanisms across numerous viruses, and the compounds identified through this research could inform general anti-viral

therapeutics. Directed by Dr. John Cavanagh, Brody's Chair of the Department of Biochemistry, this work will build on Dr. Cavanagh's proven track record of success in therapeutic innovation.

Starting with *in silico* compound screening *in vitro* modeling of infection in ECU's BSL3 laboratory, Brody's Dr. Tonya Zeczycki and Richele Thompson will evaluate models of infection and treatment using biophysical and biochemical techniques, including mass spectrometry, fluorescence spectrometry, and circular dichroism, to characterize the unique properties of the viral-host protein complex and identify chemical compounds which disrupt the interactions. Our work will provide insight into the nature of the viral-host protein-protein interactions driving SARS-CoV-2 infection and identify novel and repurposed therapeutic candidates that disrupt key viral-host protein-protein interactions important to SARS-CoV-2 infectivity and pathogenesis. In doing so, this work provides the foundation for the development of specific and effective antiviral therapeutic regimens for SARS-CoV-2. Funding from S.L. 2020-4 is being used to support this COVID-19-focused effort and expand lab capacity to accelerate research outcomes.

Strategy Two: Bringing a Safe and Effective COVID-19 Vaccine to the Public

Item: "(ii) bringing a safe and effective COVID-19 vaccine to the public as soon as possible…"

1. Focus on the logistics of vaccine delivery

The first-generation SARS-CoV-2 vaccine will be sped to market balancing the maximum benefit with the fastest deployment. The maximum impact will depend on public health leaders considering the optimal strategy for a vaccine where the efficacy may not be completely determined (the initial Salk vaccine reduced polio infections by just 50%) and where clinical trials limited recruitment of the most vulnerable populations.

In May 2020, a partnership formed between ECU and Vidant Health, led by Dr. Greg Kearney from the Brody School of Medicine's Department of Public Health and drawing on experts from ECU's Thomas Harriot College of Arts and Sciences and analysts and logistics specialists from Vidant Health. This team undertook the mapping in time and space every identified COVID-19 case in the 29-county region of northeastern North Carolina served by Vidant Health. Building on prior work to map out vulnerable populations, this team characterized the history of COVID-19 spread in the region and determined risk maps for future spread.

The project has evolved into two parallel efforts: geographic surveillance and trajectory mapping of COVID-19 in eastern North Carolina under Dr. Kearney (the COVID-GIS Team) and a review of optimal vaccine distribution under Dr. Maria Clay, Chair of Brody's Department of Bioethics (the Vaccine Distribution Team).

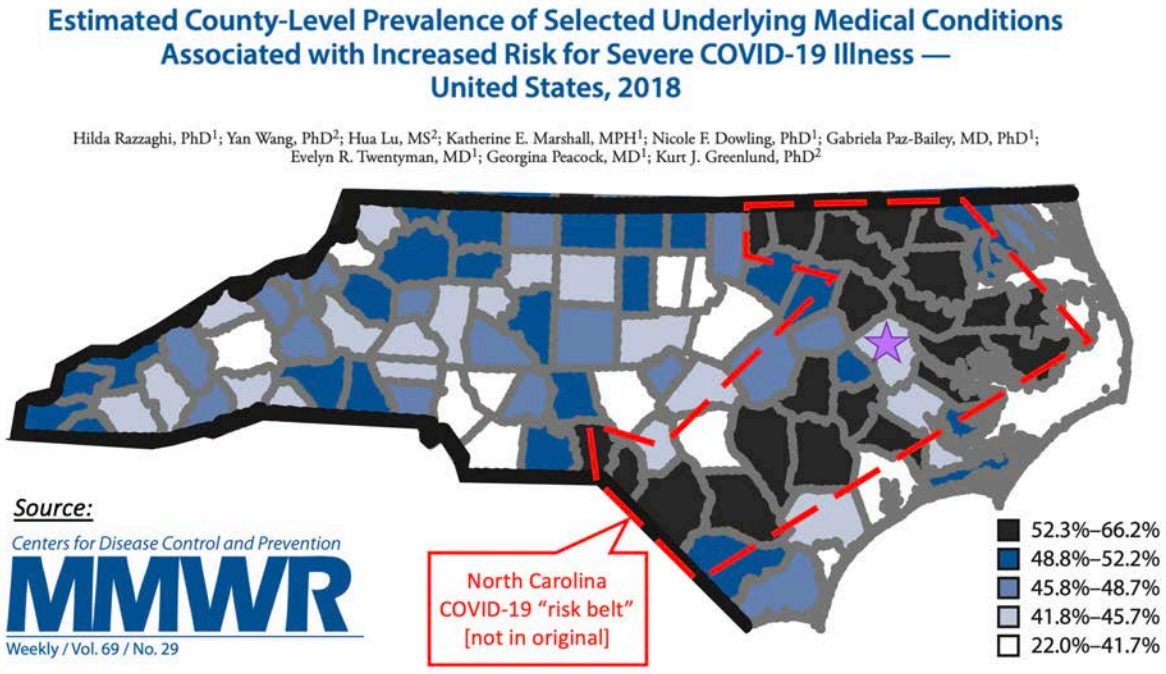

Figure 2: A CDC report identified US counties with high prevalence of underlying medical conditions associated with high risk of severe COVID-19 illness. In the North Carolina map, there is a "risk belt" that traverses the eastern region of the state. The red outline has been added to the original graphic. The star is ECU. (Source: CDC. *Morbidity and Mortality Weekly Report*. July 24, 2020.)

Geographic Surveillance and Trajectory Mapping: Health data and information are vital for monitoring and surveillance of COVID-19 in the population, anticipating the trajectory of infections across the region, and identifying approaches to use a vaccine to create an immunity-enhanced *cordon sanitaire* to slow the spread. Using data from regional clinic, hospital, and public health partners, the COVID-GIS Team is currently applying advanced geospatial analytical techniques to characterize patterns of COVID-19 spread with the goal of 1) identify existing and predict future clusters or "hot spots" and 2) prioritize geographic areas of population vulnerability of COVID-19 throughout eastern N.C. The efforts of this project will inform and guide healthcare providers and decision leaders to make data driven decisions for reducing spread of COVID-19, target population areas for interventions, including distribution of a vaccine when it becomes available, and prioritize prevention strategies.

Specific attention will be paid to the region's socio-vulnerable population areas of concern considering poverty, socio-economic status, and medically underserved and healthcare provider shortage areas. Such communities today have been found to report high rates of risk factors for severe illness when infected with COVID-19 and in North Carolina they are concentrated in the east region (Figure 2).

Optimal Vaccine Distribution: While COVID-19 diffuses across the nation and penetrates vulnerable regions, clinical trials of vaccines are progressing, and the likelihood is that a viable COVID-19 vaccine is imminent. Hence, it is imperative that protocols for optimal vaccine distribution be prepared, addressing impact, logistics, and ethical considerations. Between production volumes and logistical considerations of distribution and administration, it is highly likely that vaccine availability will be slow to meet population demands. While national entities (e.g. CDC, National Academies of Sciences, Engineering, Medicine) may formulate general guidelines, it is imperative that local vaccine distributions guidelines be outlined, especially with a goal of identifying infrastructure and resource needs to ensure that ethically endorsed principles achieve desired vaccination distribution effects. A Vaccine Distribution Team has been formed whose efforts will inform decision makers and local leaders to better align distribution mechanism, ethical values, and desired outcomes.

An ethical framework is necessary to address such issues as expanding vaccine access into populations not included in the clinical trial. Individuals who are extremely vulnerable to severe COVID-19 are also typically excluded from clinical research because of their fragile health, and so weighing the risks and benefits of vaccine administration, and the determination of a "tipping point," when post-approval evidence supports an expanded indication, are crucial to mitigation efforts.

This project will utilize historical literature and protocols, emerging documents and guidelines, and broad partnerships to address the following:

- Identify principles that have been used in past vaccine distribution guidelines, and currently proposed national guidelines;
- Evaluate these approaches in the context of the existing social and cultural foci, as applied to citizens of eastern North Carolina;
- Identify potential barriers to implementation of COVID-19 vaccine distribution to prioritized target groups informed by the geographical mapping project;
- Prepare a generalized approach to evaluating vaccine safety, efficacy, and availability parameters in advance of final COVID-19 vaccine trial results;
- Apply this framework to ethical and logistical issues to the available safety and efficacy evidence upon FDA approval of the first COVID-19 vaccine and inform targeting of initial vaccine distribution in eastern North Carolina; and
- Update the guidance as new evidence and subsequent generations of vaccines become available.

Success to date: Two teams have formed focused on the parallel efforts. Case information has been secured across the region through diverse partnerships with clinical laboratories, providers, and public health offices. Infrastructure and systems for temporal-spatial mapping of cases has been put in place and draws on data gathered through data sharing agreements. The Vaccine Distribution Team has conducted a survey of the scientific literature on vaccine distribution, expanding beyond journal articles and monographs to include diverse informal resources and developing standards. The Vaccine Distribution Team and COVID-GIS Team have

formed a subgroup focused on modeling vaccine distribution efforts in the context of the geography of COVID-19 in eastern North Carolina. The Vaccine Distribution Team has also identified parallel efforts in other states and regions and have established points of collaboration.

A key resource as this effort moves forward will be the cross-campus North Carolina Agromedicine Institute, housed at East Carolina University. The NCAI is engaged in work to provide support to farm workers, foresters, and fishermen through the pandemic, and insight from NCAI leaders is informing the efforts of the Vaccine Distribution Team.

2. Basic science efforts to advance vaccine development

Support from S.L. 2020-4 is supporting two important projects to advance our understanding of COVID-19 vaccines, under lead investigators Dr. Mark Mannie and Dr. Rachel Roper, both holding appointments in ECU's Department of Microbiology and Immunology.

Dr. Mannie is currently the principal investigator on a National Institute of Allergy and Infectious Disease R01 grant to study anti-inflammatory mechanisms. One focus of his research, FOXP3-positive T cells, represents a mechanism implicated in the COVID-19 cytokine storm. The cytokine storm is well established mechanism for COVID-19 mortality. Dr. Mannie's research on "infectious tolerance," the process of moderating the immune response to infection in order to limit potentially harmful immune system response, has direct application to mitigating COVID-19 morbidity and mortality and could inform development of second-generation vaccines to mitigate the consequences of infection. Insight gained from Dr. Mannie's work would inform approaches to future outbreaks of many novel pathogens.

Dr. Roper is one of the leading microbiologists studying coronaviruses and was the senior scientist in the first sequencing of the 2003 SARS coronavirus, publishing a paper on the genome of the SARS-CoV virus that has received over 1,000 citations. Dr. Roper has received a grant to support SARS-CoV-2 research using animal models, and funding from the appropriation will supplement and extend this work, with the goal of achieving better insight into vaccine mechanisms faster so as to be available to inform public health interventions sooner.

Working with ECU's School of Dental Medicine, Dr. Roper is also piloting a saliva-based testing platform for surveillance of COVID-19 through dental clinic facilities across North Carolina providing care for underserved, diverse and minority populations, evaluating the efficacy of federal safety dental service guidelines, and acting as a sentinels for community spread of COVID-19. The research will develop improved testing protocols including the use of wearable technology devices and computer algorithms to aid in monitoring and predicting health and infection risks, and evaluation of the immune state and responses to COVID-19 for early identification of patients who may develop critical illness.

Strategy Three: Community testing initiatives

Session Law 2020-4 §24: *"(iii) community testing initiatives"*

1. Expanding the capacity of the Brody School of Medicine Pathology Department

Dr. John Fallon, Chair of the Brody School of Medicine's Department of Pathology also serves as Chief of the hospital laboratory at Vidant Medical Center. Dr. Fallon is a widely recognized state leader in COVID-19 testing. Since the start of the pandemic, Dr. Fallon has continuously expanded the lab's capacity. Through Dr. Fallon's efforts, the VMC lab has continuously maintained a track record of delivering clinical testing results in less than 24 hours, facilitating useful contact tracing and isolation protocols.

With the first established re-infection with SARS-CoV-2 identified in Hong Kong, the importance of viral sequencing was highlighted. With the probability of near-term eradication of SARS-CoV-2 decreasing, the genetics of the virus will become increasingly important to clinical outcomes. Dr. Fallon is an established leader in molecular pathology and with support from S.L. 2020-4, Dr. Fallon is augmenting the department's clinical genetics core in order to track the history of viral mutations impacting our region and to allow the study of genetic factors linked to extrema in clinical outcomes.

Through August 28, Dr. Fallon's lab had completed over 90,000 RT-PCR tests on over 72,000 unique patients, with over 9,000 tests completed over the prior seven days. In total, the VMC lab has diagnosed over 6,100 unique patients as infected with SARS-CoV-2. This capacity is important as rural and remote counties often suffer from insufficient testing. For example, while the North Carolina Department of Health and Human Services currently lists a statewide positive rate of 7.4% in COVID-19 testing, Bertie county's positive rate is 10.3% and Duplin's is 14.9%.

2. Support for cohort studies

Study of Exposure, Infection, and Recovery: Drs. Suzanne Lea and Arron Kipp, faculty in the Brody School of Medicine's Department of Public Health are conducting cohort studies to supplement clinical care for insight into disease transmission. Dr. Kipp is leading the eastern North Carolina arm of the statewide Community Testing and COVID-19 Testing Study, or ComPACT, initiated with support from the CDC. The ComPACT study is targeting recruitment to rural, diverse, and medically underserved individuals in our community. Using support from S.L. 2020-4, Dr. Lea is conducting a parallel study focused on students. Given the events of August, this study, designated PiratePACT, is especially important as recruitment is focusing on students who are staying in their off-campus housing in Greenville rather than returning home. The goal of this supplemental arm of the ComPACT study is to understand the interaction between individual characteristics and the spread of COVID-19 by tracking exposures and attitudes in a student population while tracking biomarkers for infection and recovery.

Outpatient Follow-up Study: A second follow-up study is being conducted to track symptoms and recovery in the non-hospitalized SARS-CoV-2 positive population identified through Brody's faculty practice, ECU Physicians. This study is under the overall direction of Brody's Associate Dean for Research, Dr. S. Russ Price, and is being structured to allow medical students to participate in COVID-19 research. The study involves weekly telephone follow-up calls with infected individuals, with questions assessing overall health, the burden of illness, and economic hardship associated with a COVID-19 diagnosis. This study was started in May of 2020 and is currently tracking 311 individuals who completed nasopharyngeal testing through ECU Physicians. During the Spring, nine students from North Carolina Central University's Clinical Research Program completed their degree requirements for internships supporting this study. Brody medical student involvement was held until after the students returned to campus in August.

Strategy Four: Additional Research and Activities Addressing COVID-19

Session Law 2020-4 §24: *"(iv) other research and activities related to COVID-19"*

1. Infrastructure for Basic Science Research

BSL3 Lab Upgrade: The Brody School of Medicine's Department of Comparative Medicine, under Chair Dr. Dorcas O'Rourke, required renovation of its biosafety level 2 laboratory to accommodate the biosafety level 3 (BSL3) pathogen, COVID-19. With support from S.L. 2020-4, Dr. O'Rourke worked with ECU's facilities department to upgrade two laboratories with safety and security infrastructure necessary for a BSL3 laboratory, including support for *in vitro* and animal research. The upgrade included upgraded airflow and filtration, improved seals to doors and fixtures, BSL3-rated animal housing, improved sterilization, an airlock-style entrance, and enhanced cameras and security. When complete, two labs will be renovated, both as multi-investigator shared lab space. All of the studies listed above employing actual SARS-CoV-2 virus, whether in cell or animal modes, will be conducted in this lab space.

As of this report, the upgrade nears completion. The air handler and ductwork have been upgraded to meet the BSL3 standard and facilities for pathogen storage have been prepared. Security systems have been upgraded to meet the required standards with pressure monitors installed to ensure filtration systems are functioning, cameras installed with overlapping coverage, card readers for access control installed, and independent wired telecommunications for secure equipment monitoring. Network coverage has been upgraded to support smart animal housing with self-contained monitoring.

Histopathology Resources for COVID-19 Research: To compliment the upgraded BSL3 facilities, histopathology capacity for processing and evaluating large numbers of tissue samples from animal tissue infected with a dangerous pathogen was necessary. Dr. Peter Koch, Chair of the Brody School of Medicine's Department of Anatomy and Cell Biology has experience in building a histopathology core lab and has led this capacity expansion in collaboration with Dr.

O'Rourke. New equipment, currently on order, will support simultaneous processing of multiple samples, increasing the ability to compare case and control samples; automated slide staining to increase the safety and speed of sample staining; enhanced microscopy capacity including multi-headed microscopes for teaching purposes; and high-resolution imaging tools.

2. Supporting high-risk populations

At-Risk Diabetic Cohort: Both diabetes and obesity are significant risk factors for poor outcomes with COVID 19. Unfortunately, management of diabetes with insulin contributes to obesity in type 2 diabetes, the most common form in eastern North Carolina. The Nephrology Division of Brody's Department of Internal Medicine has an established investigator focused on the conversion of type 2 diabetes patients to non-insulin therapies. With support from S.L. 2020-4, the division has been able to allow this investigator to focus on managing these risk factors in this to addressing this problem full time which greatly expands his access to this high-risk population.

COVID-19 and Neurovascular Risk: Emerging evidence has demonstrated that while the acute risk of SARS-CoV-2 infection is respiratory, the chronic effects after infection are vascular. Eastern North Carolina is well established as a region of high stroke risk, and the long-term effects of SARS-CoV-2 infection in individuals at risk of stroke are unknown. The 1918 H5N1 flu pandemic was conclusively linked to neurological sequelae that manifested in some individuals as late as the 1950s. Brody's Department of Medicine, under Chair Dr. Paul Bolin, has assembled a group of experts in this area to create a tracking tool to follow these patients over time.

3. Personal Protective Equipment Innovation and Improved Training

PPE Innovation: Since the start of the pandemic, the gold standard N95 respirator, with proven capacity to minimize viral exposure even high-risk environments such as the COVID-19 ICU, has been in short supply. The high demand for N95 NIOSH approved respirators has created need to finding alternative respirators with similar efficiency. Dr. Sinan Sousan, an ECU faculty member holding a joint appointment in Brody's Department of Public Health and the North Carolina Agromedicine Institute has studied air filtration in agriculture and has provided his expertise to this challenge. Leading a joint team of scientists and physicians, Dr. Sousan has undertaken a project to study filtration efficiency, analyze factors in face mask effectiveness, and rapidly produce a candidate prototype respirator. Dr. Sousan's lab will build on his established work in filter testing to evaluate the efficiency of fabrics that are advertised as possible replacements for the N95 respirator, with the goal of rapidly producing a 3D-printed framework to house a multilayer filter fabric yielding an alternative for the N95 respirator that can be used by healthcare professionals.

Improved PPE Training: The aim of the project is to ensure that health sciences students enter clinical spaces with knowledge and skills in PPE usage so they can keep themselves and their

environment safe and to answer patient/client questions relative to PPE. Initial success resulted in the expansion of the project to sharing learning material with students and faculty on the main campus to contribute to an environment that learns and practices sound PPE behaviors. S.L. 2020-4 support is being utilized to partially fund for program development, program delivery, and supplies.

With the launch of this project, diverse PPE training initiatives across the region have been consolidated. First conceived to focus on safeguarding students in the Brody School of Medicine, the efforts of the Eastern AHEC, Vidant Medical Center, and ECU's colleges of Nursing and Allied Health Sciences, School of Dental Medicine, Division of Academic Affairs, and the faculty practices have all been combined under this umbrella effort. The groups across campus and the region will share a common curriculum on PPE safety.

4. Telehealth Expansion to Rural Eastern North Carolina

East Carolina University received statewide recognition for innovation in telehealth through Dr. Sy Saeed's O. Max Gardner award from the UNC System in 2019. Dr. Saeed, Chair of the Brody School of Medicine's Department of Psychiatry and Behavioral Medicine, developed a hybrid model of telepsychiatry linking clinical care and telemedicine and enabling the critical provision of psychiatric care to small, rural emergency departments that often struggle to provide psychiatric evaluation.

COVID-19 has exposed a similar challenge in the need for expert consultation on follow-up care across the region for at-risk and chronic sequelae of SARS-CoV-2 infection. Eastern North Carolina was replete with rural and medically underserved counties and the pandemic has exacerbated already poor access to healthcare. Correcting this is a critical need. In a cross-departmental collaboration led by Dr. Paul Bolin, Chair of Brody's Department of Medicine, and in collaboration with Dr. Saeed, the team will create multiple in person and virtual clinical sites in rural eastern North Carolina. These clinical sites will build on Dr. Saeed's NC-STeP model, with a local staff of medics and EMTs supported by ECU specialists through telemedicine. This model launched early in the pandemic to support specialized care for COVID-19 patients across the region with infectious disease and critical care specialists. Expansion of this model is underway to allow all medical specialties and dental medicine to deliver care into rural and remote communities. Two key challenges impact our region: access to care, a chronic challenge in our region exacerbated by COVID-19; and a high prevalence of risk factors for severe COVID-19. Poverty, economic hardship, and distrust of the healthcare system compound the dearth of providers in the region. This hybrid model, based on local, low-fee providers supported by remote consultants will project high-quality care further into the region and support in-person opportunities for health care where our patients live and work. Opportunities exist to partner with both industry and agriculture allowing the program to remove many of these barriers for our most vulnerable. COVID-19 has exposed the fragility of our region's economic progress, and this program has potential for a dual benefit in ENC. Outreach clinics will focus on

impacting six of the most important risk factors for severe disease, thus benefitting a vulnerable population far beyond mitigating the impact on COVID-19.

IV. Financial Spreadsheets

The following are unaudited financials for expenditures of funds provided under State Law 2020-4 to the Brody School of Medicine. These financials are computed on a cash basis and do not reflect charges based on commitments or contractual obligations if payment has not been made.

Brody School of Medicine at East Carolina University

COVID-19 Special State Appropriations Research Projects

Budget and Expenditures by Strategy

	Total budget allocation	Expenditures through 8/30	Remaining funds
Strategy 1: Enhancing innate immunity	3,906,953	18,052	3,888,901
Strategy 2: A safe and effective vaccine	2,007,550	51,215	1,956,335
Strategy 3: Community testing	3,338,168	37,491	3,300,677
Strategy 4: Additional research & activities	5,747,329	1,528,961	4,218,368
Total	15,000,000	1,635,719	13,364,281

Monthly reports are provided to the North Carolina State Budget Office.

V. Closing

The administration and faculty of the Brody School of Medicine at East Carolina University, a campus of the University of North Carolina System, are humbled by the challenge that the COVID-19 crisis has brought to our region and our communities. The group has endeavored to bring all of the clinical and scientific resources we can muster to fight the disease and to make our campus safe for our students while we continue to train the next generation of healthcare professionals. We express our deep and heartfelt gratitude to the General Assembly of North Carolina for entrusting the Brody School of Medicine with the support that has allowed us to expand our clinical initiatives, leverage our best science to generate new insights, and deploy our public health resources to better fight COVID-19 in our communities and our state, and to help contribute to the world-wide effort.

This report was prepared on behalf of the Dean of the Brody School of Medicine, Dr. Mark Stacy under the direction of Vice Dean Peter Schmidt. Questions and comments may be directed to Dr. Schmidt by electronic mail, schmidtp18@ecu.edu, or by phone, 1-252-744-7400.