

Dear Faculty, Staff, Fellows, Residents and Students,

Here we are again, writing to you for the fourth time since the coronavirus crisis began. So much has happened over that time. With massive planning and exhaustive work by many of you, we have mobilized our teams at WashU and BJC and worked in collaboration with the other St. Louis-area hospital systems, as well as the city, county and state governments, to tackle the surge of patients with COVID-19 in our community. We can now see definite signs of progress, including recovery of severely affected patients and a smoothing out of the surge. As we begin to allow ourselves to think about the future, there are still big questions – far too many of them – and somehow we still feel vulnerable. The virus, SARS-CoV-2, is a formidable foe because of its unique abilities to spread and its acute lethal potential.

While all of this has been going on, a large group of our faculty has rapidly mobilized to try to address this virus and our future through research efforts. The faculty here at WashU have long understood the looming threat of deadly viruses and the likelihood of pandemic in an increasingly global world. Over many years, a number of internationally renowned members of our faculty in the areas of virology and immunology have focused on advancing countermeasures against these infectious threats. The talent in these groups is rare and unmatched at any academic medical center in the country, and they are now working tirelessly with colleagues across the campus – particularly faculty in the clinical laboratories of the Department of Pathology & Immunology, as well as in the McDonnell Genome Institute – to mount our research response to CoV-2.

Just as it has been uplifting to see our clinical faculty and staff mobilize for the needed clinical care, it is thrilling to see how our research teams are responding. Collectively, this group of laboratories that comes from our deep bench is advancing efforts to develop new diagnostics, therapeutics and vaccines, as well as to define the basic elements of SARS-CoV-2 pathogenesis, the correlates of a protective and maladaptive immune response, and the genetics of host susceptibility and viral virulence.

There are many academic and industry laboratories around the world now working on this problem, but we cannot assume that others are going to succeed and we need multiple different strategies to maximize our chance of success. Scientists at WUSM are using their unique expertise to advance novel strategies for vaccine development. Dr. Sean Whelan in particular has led efforts to generate a chimeric virus that appears identical to COVID-19 on the outside but contains the replication machinery of the livestock pathogen vesicular stomatitis virus (VSV) on the inside. That particular livestock pathogen does not cause disease in humans, and formed the basis for the Ebola vaccine in current use, and is therefore an appealing platform for a future Co-V2 vaccine.

Ideally, the first step for launching any vaccine or therapeutic drug intervention is to test it in one or more animal models. Preclinical testing in an animal model is a time-tested approach to improve efficacy and safety. Here at WashU, our own Dr. Michael Diamond and his team are ahead of the field in developing the first hightthroughput animal model of COVID-19 in mice using genetic engineering approaches, as well an approach in which viral adaptation is promoted through passage in an immunodeficient background. Michael and his team took an analogous approach in 2015-16, when they developed the first mouse model of Zika infection, another pathogen to which mice are not naturally susceptible. At that time, they were able to identify an antibody that is now used as part of a diagnostic test for the disease. Michael and his lab offer just one example of many WUSM scientists drawing from a wealth of experience investigating infectious diseases. Any day now, other scientific collaborators from departments across the campus will begin testing therapeutic interventions in the new mouse model, including FDA-approved drugs that can be repurposed for COVID-19, novel compounds, and antibodies that could be used for immunotherapy.

Widespread testing will be the key to managing the outbreak and getting our country going again. We need a simple and effective test platform to identify at the earliest possible stage those who are infected, and those who are most likely to have an acute response to the infection. This is being tackled with a three-pronged approach. First, we have our world-class talents in the Immunobiology program and the Bursky Center for Human Immunology & Immunotherapy Programs to develop the serologic basis of the immune response to coronavirus. Second, we are deploying the McDonnell Genome Institute to develop a highly sensitive, scalable polymerase chain reaction (PCR) based test for virus, using saliva, which will allow self-collection and avoid the necessity for nasopharyngeal swabs and reagents that are in limited supply. Finally, we are capitalizing on a group of investigators in the Department of Pathology & Immunology to miniaturize the assays so that hightthroughput handling of samples is scalable for rapid reporting of results from large populations. This combined approach will give us a way forward, forming the first, necessary line of defense for slowing the spread of the disease and reenergizing our flagging economy. Our investigators expect their tests to be easily exportable to other cities, allowing us to share our expertise with the world.

This is the WashU way: expertise paired with ingenuity and extensive collaboration. We have always prided ourselves on being a collaborative institution and have both attracted world-class researchers to WashU and kept them here on the strength of our commitment to fostering collaboration. Our efforts to respond to COVID-19 will be the truest test of that collaborative spirit, but already we are seeing positive signs as different labs work together to meet specific goals, and individual PIs put their own projects aside to contribute to the public good. This spirit of selfless collaboration is why, for example, we were able to get a clinical trial up and running in a record 12 days.

This is a formidable challenge, probably the toughest one many of us have faced in our careers, and it requires that we not only draw upon our vast research capabilities but that we do so differently, and more rapidly, than ever before. We are being asked to be adaptive, light on our feet. Could there be a more profound test of our identity as an academic medical center? Never have our mission and purpose been so evident as this crisis highlights the critical importance of the work in which we have been engaged for years. As an academic medical center our unique

purpose marries clinical care of the sickest and most vulnerable today and using our scientific know-how to develop even better ways to prevent and treat their illnesses for tomorrow. In a time when challenges to science and the dismissal of facts have been woefully widespread, we now face a problem that demands solutions grounded in data and the scientific imagination. This virus, and our response to it, have revealed the extent to which we are guardians of public health, activated in times of crisis but always working behind the scenes, even while no one is paying attention.

They are paying attention now. We are facing a potent challenge for our scientific capabilities, an easily transmittable virus that has enormously intelligent ways of creating turmoil. But we have spent years laying the groundwork for our response. While all eyes may be on us in this particular moment, any discovery or treatment will be the result of that groundwork, research we are now harnessing to help our community and the rest of the world. This is a sacred responsibility. As always, we are honored and humbled to lead such an unparalleled group of scientists as they work tirelessly to help us find a way forward out of this morass.

Sincerely,

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Executive Vice Chancellor for Medical Affairs and Dean

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Chancellor