DATE: Tuesday March 17, 2020

TO: Our DNA Company friends and relatives

RE: Addendum to our COVID-19 message

Disclaimer: This missive is meant solely for educational purposes and is not intended as therapeutic or diagnostic advice. All diagnostic and treatment decisions return to your licensed primary healthcare providers.

Dear friends and colleagues, we did not anticipate the overwhelmingly positive feedback we received from our first message on the COVID-19 outbreak. It reminded us that accurate and moderated responses in times of trial are always needed. To this end, we will be releasing addendums that summarize the most up-to-date and validated insights available from the global scientific community, as well as answer the most pressing questions we receive.

- One of the most asked questions we have received relates to how long coronaviruses can survive on surfaces (with specific relevance to COVID-19).

In order to answer this question, we must first understand that viruses require a living host to survive and reproduce. Said simply, unlike most other micro-organisms, viruses typically cannot survive indefinitely outside of a living cell. Dr. Neeltje van Doremalen, a virologist at the US National Institutes of Health (NIH), and her colleagues at the Rocky Mountain Laboratories in Hamilton, Montana, are some of the first to study the life cycle of SARS-CoV-2 outside of human cells (please note that some scientists are differentiating between the name of the current novel coronavirus and the infection it causes. In order to keep to the best nomenclature standards, moving forward we will refer to the virus as SARS-CoV-2 and to the disease/pandemic it causes, as COVID-19).

The data collected by Dr. Doremalen and colleagues demonstrate that:

1. SARS-CoV-2 can survive in the aerosolized droplets of our sputum (the saliva and mucus we emit when we cough, sneeze or even when we simply speak or exhale vigorously). These microdroplets of our sputum can remain airborne for several hours, and within them, the SARS-CoV-2 virus can stay alive for up to 3 hours. One would imagine (correctly) that this does not bode well for being in poorly ventilated, densely populated environments for prolonged periods during this outbreak.

2. Dr. Doremalen's study further concluded that the SARS-CoV-2 virus can survive for much longer periods once they settle – up to 24 hours on cardboard surfaces and up to 2-3 days on plastic and stainless-steel surfaces. Interestingly, copper seems to possess an inherent anti-viral property – killing the SARS-CoV-2 virus within 4 hours of contact.
3. The porous and fibrous nature of most clothing items makes studying the survivability of SARS-CoV-2 on them very difficult. Some studies suggest that the virus has a shorter survivability on clothing fabrics, but those data are far from conclusive. It would be more conservative to assume that the virus can survive on clothing for at least several hours (until otherwise clarified)

Now that we have a sense of the survivability of the SARS-CoV-2 virus outside of a host (human cells), let's consider some practical ramifications.

Wearing a mass may very well protect you from passing on the virus through your own emitted sputum (should you be carrying the virus) or from contracting it yourself via airborne transmission from others. However, aerosolized droplets can be as small as 1-5 micrometres in size – about 1/30th the width of a human hair. Accordingly, if you choose to wear a mask, you should ensure that it meets the appropriate filtration specifications. Importantly, masks do not protect you from touching surfaces upon which viral particles have settled, nor do they prevent you from transporting them to other surfaces (or other humans).

The take home point here is that wearing a mask does not replace proper hygiene habits, nor does it replace an intelligent awareness of your environment. We cannot stress this enough. Engender in yourself and your loved ones, a thorough handwashing habit when leaving places of high human traffic – shops, public transportation etc – and when returning home, or to your workplaces.

It is likely worth a gentle reminder of a few of the ghastliest surfaces we often overlook...none of which are in bathrooms (which of course are germ zones):

1. Handrails. The handrails of escalators have been shown to be some of the filthiest surfaces in communal areas
2. The containers that are used to place your belongings in as you pass through airport security are quite literally filthier than the toilets of those same airports
3. Your cell phones are subject to relentless sputum bombs from your mouth day in day out
4. Your laptops and other mobile devices

While on the topic of surfaces and cleanliness, the following have been shown to rapidly inactivate coronaviruses:

1. ~70+ % alcohol solutions
2. 0.5% hydrogen peroxide

3. 0.1% sodium hypochlorite
4. ¼ cup of bleach per 1 gallon of cold water. Please note that a diluted bleach solution should be used within 24hours, as it loses its disinfecting properties over time

Please exercise extreme caution when interreacting with any of these agents. Under normal circumstances we would not even recommend some of these disinfectants. However, these are not normal circumstances.

- *Another repeated question we have been asked is in regard to the infection cycle of COVID-19 and the concept of viral shedding*

In our first missive we highlighted that the SARS-CoV-2 virus seems to enter human cells by binding to the ACE2 cell surface receptor. Think of the ACE2 receptor as the door through which the coronavirus enters the human cell. Unsurprisingly, these receptors are expressed on cells of the lower respiratory tract. Interestingly, these receptors are also expressed on cells of the cardiovascular system (more on this later).

To recap, the SARS-CoV-2 virus binds and enters human cells via the X-linked *ACE2* gene product (which is an enzyme/receptor). Because the *ACE2* gene is X-linked, it is likely differentially expressed in women and men – women have 2 copies of the *ACE2* gene, while men have only 1.

The role of the *ACE2* gene in the COVID-19 pandemic is definitely something that we will be keeping a closer eye on in the coming weeks/months.

(*A point of note: a number of clinicians have mistaken the ACE2 gene for the primary ACE gene. However, the primary ACE gene is located on chromosome 17...and should not be confused with the ACE2 gene...which is located on chromosome X*).

<u>While it must be stressed that these are extremely early observations:</u>

Dr. Zunyou Wu, MD, PhD, chief epidemiologist at the Chinese Center for Disease Control and Prevention, has presented data showing that <u>more than 40% of people with severe COVID-19 infection had baseline hypertension and cardiovascular disease</u>. Among those with severe illness, the next most common comorbidity was diabetes, which was about half the rate of those with underlying cardiovascular disease. Moreover, more men appear to present with more severe symptoms than women.

Does the difference in expression of the *ACE2* gene in men and women explain why there appears to be a preponderant morbidity and mortality in males? The epidemiologic data surrounding the COVID-19 outbreak is still extremely sparse and it would be irresponsible to draw premature conclusions. However, it would be equally irresponsible to leave any strong associations unexplored. The central role the ACE2 receptor plays in both the infectious cycle of the SARS-CoV-2 virus as well as in the cardiovascular system; the male/female dimorphism of the expression of the *ACE2* gene; the apparent preponderance of male morbidities and mortalities; and the confounding comorbidity of cardiovascular disease; all suggest that this is

an angle or query that must be further explored.

Moreover, can other genes involved in the risk of chronic inflammation, cardiovascular and pulmonary disease be used to stratify risk of severity in the COVID-19 infected population?

At The DNA Company we have studied the novel genomic underpinnings of chronic inflammation, cardiovascular and pulmonary disease susceptibility in thousands of patients. We intend to aggressively evaluate these insights to determine if they might allow for a better stratification of COVID-19 infected patients. As we discussed in our original missive, it is not the general severity of the COVID-19 outbreak that is concerning. Rather, it is the strain on our healthcare system that is alarming (see below). Any – stress any – insights that better stratify the at-risk COVID-19 infected population will likely not only impact patient survivability, but radically influence the saturation capacity of our healthcare system and response.

Regardless of where the research on ACE2 and underlying cardiovascular comorbidity leads us, what we do understand is that once the SARS-CoV-2 virus enters the human cell it shows its true disturbing colors. Dr. Wolfel and colleagues from the Institute of Microbiology, Munich, Germany, have shown that the SARS-CoV-2 virus co-opts the resources and inner machinery of the human cell in an alarmingly fast manner. All viruses co-opt their host cells to reproduce. Once they have drained the resources of their host cells, they then erupt from the host cell in all the glory of their offspring (trust me when I say it's not an image you want to ponder for too long). This phenomenon is known as viral shedding. It is the viral shedding that populates your sputum with millions of viral particles as per our discussion above. The SARS-CoV-2 virus seems to be shedding faster than previous coronaviruses – and if very early studies are confirmed – at a rate of 1000X more than the previous SARs coronavirus. Said simply, COVID-19 infected patients are apparently spewing 1000X more viral particles per volume of sputum than patients infected with previous coronaviruses...and they are doing so often before they are even symptomatic!

Now to be clear, and to re-emphasize, the degree of viral shedding does not equate to the severity of the viral infection. We are still dealing with a virus, which for the vast majority of infected individuals, will lead to only nominally more severe symptoms than the common flu (if even that). However, for a percent of the infected population (estimated at about 3-4%), COVID-19 will be a life or death struggle. When combined with the extremely high rate of transmission (as addressed above) and the symptomologies experienced by those with severe manifestations of the infection (pulmonary and cardiovascular co-morbidities), it is simply a numbers game before our healthcare systems become saturated, and we lose the ability to care for not only COVID-19 patients, but acute trauma patients, child-birthing women, cancer patients etc., all of whom will demand care from the very system drained by this pandemic.

With these further insights, the conclusion of our initial missive is all the more relevant and poignant:

With a mature and purposeful approach to limiting the spread of the COVID-19 outbreak, we can keep not only ourselves and our loved ones safe, but our communities, and the most at risk within them, as well. This mature approach will, and must, require a sense of communal

belonging and responsibility. The healthy and strong amongst us must be aware of the weaker and less resilient. The vast majority of COVID-19 cases will be no more severe than the common flu. The primary concern is not the contraction of the virus. The primary concern is its unchecked spread and the related catastrophe this can have on our urgent care/healthcare system.

To this, we will now add another primary concern and objective:

- *We must become better at stratifying and predicting the at-risk population*

Better patient stratification is the only way our healthcare system can hope to accommodate the simultaneous demands of acute trauma care, chronic diseases and pandemics.

As always, on behalf of The DNA Company, I wish each of you the best of health and wellbeing. We are available to answer your questions should you have any.

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