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More on the ACE2-Related Asian COVID-19 Susceptibility Hypothesis

James Lyons-Weiler, PhD – 2/16/2020

SCIENCE IS FOR ASKING QUESTIONS. When people started posting online the idea that "Asians", especially male "Asians", and perhaps people with the "Han genome" are generally more susceptible to morbidity (serious illness) and mortality (death) from SARS 2 infection leading to COVID-2019, the natural question then becomes "where is this coming from" and "what data are there to support this"? The alleged implications are that the risk of serious illness and death from SARS 2 infection might imply a that the SARS 2 virus is a bioweapon, made by the US, that targets "Asians" or people with the "Han genome".

When scientists want to understand who is at risk, sometimes they look at genetic risk. While the ACE2 is gene is related to that for ACE, and variation in both genes sometimes co-contribute to risk of certain health outcomes (e.g., thyroid cancer, hypertension, kidney disease), ACE and ACE2 encode distinctly different proteins. So my earlier post that variation shared among ethnic groups in ACE would tend to rule out the logic of a genetically targeted bioweapon, the genetic variation I described was for ACE, not ACE2. The general lesson, however, still applies: any high-frequency

genetic variation (inherited variation) in ACE2 would be shared across many ethnic groups, so it, too, would make a terrible bioweapon.

The confusion stems from a simple human error made in a Reddit forum where those poster shared a link to a study from 2007 on geographical variation in the "ACE II" genotype. As I explained in my article, ACE II is not ACE2 but instead refers to the ACE I/I genotype, where individual receive one allele at the ACE locus (not the ACE 2 locus) from mom, and one from dad. The other known allele is the D allele, and so there are three possible genotypes – I/I, I/D and D/D – that a person can have. Since the original Reddit post confused ACE2 and "ACE II", I hope the post, which provides a basic lesson on inheritance patterns of genetic variation, clarifies.

But Still, Why the Focus on ACE2?

ACE2 is known to be a point of cellular entry for B-coronaviruses, notably SARS. There is this study (***"The novel coronavirus 2019 (2019-nCoV) uses the SARS-coronavirus receptor ACE2 and the cellular protease TMPRSS2 for entry into target cells"***) that shows, using data from a handful of people from China, that one of the males had a much larger amount of ACE2 gene expression in his lung tissue. Gene expression is a function of genetic variation, environment, and developmental programming in any tissue. In the studies I have been involved in that focus on gene expression studies (using either RNASeq or whole genome gene expression arrays), studies this small are called "pilot projects" and whole-population generalizations away much larger studies with data from many, many more patients. Even then such generalizations are only warranted if the studies can be replicated.

But let's say that (hypothetically) that ACE2 is more highly expressed in Asian males (again, hypothetically) and reason out whether it makes sense as a marker for a targeted bioweapon. Some facts about ACE2 might aid in quelling the idea that any country could target another using genes that are more highly expressed in tissues in people from one ethnic group than others:

(1) ACE2 is also expressed in every other human being on the planet;

(2) ACE2 is expressed in many different tissues, the variation among different ethnic groups is largely unknown.

So, ACE2 variation in the study is not an indication in any way that SARS 2 is expected to more deadly to Asians, or to Asian males.

Further, another study showed that compared to SARS, SARS-2 more weakly binds to ACE2, likely due to conformational differences in the protein that may be reflected in the putative pathogenicity motif signal IPAK has discovered. Our analysis indicates

that SARS 2, or at least its spike protein, is an OLDER version of the SARS virus. And while we have not yet ruled out recombination in the wild entirely (although others were quick to rule it out), we have evidence that falsifies the idea that laboratory recombined Spike proteins are in any way involved in the origins of SARS 2.

So, in sum, the very small paper and the underlying knowledge base on the fundamentals of genetics and gene expression patterns cannot be used to support the hypothesis that SARS 2 is engineered to target Asians.

Why Is the Mortality Rate So Low Outside of China?

The current mortality rate outside of China is very low, I estimate around 0.005%, compared to the 2.3% rate in China. Most if not all of the deaths outside of China have involved Chinese citizens who have traveled abroad.

Current hypotheses include that a covert SARS vaccination program was included in the national mandatory vaccination program started on Dec 1, 2019 that happened to involve a secondary true outbreak of Coronavirus with secondary exposure. Under such conditions, the animal models clearly show that vaccination against SARS spike proteins lead to high rates of morbidity and mortality, especially in older mice. No children seem to be dying in China, consistent with them being excluded from a large-scale initial Phase II or Phase III trial. Mortality appears highest in Hubei and Wuhan as well. We know a Phase I trial against SARS was conducted with 120 people by Sinovac around 2007.

Another possibility is that a vaccine used by the Chinese has weakened their response to an otherwise mild coronavirus infection. SARS 2 binding to ACE2 is weaker. Thimerosal inhibits ERAP1. Vaccination with aluminum hydroxide containing vaccines might induce autoimmunity in the lungs. All of these factors could play a role in making vaccinated individuals more susceptible.

A third possibility is that people in that geographic region who had prior SARS infections might be less able to fight off SARS 2 simply due to original antigenic sin from infection. Toronto, Canada, take note.

Either way, as SARS 2 spreads around the world, the medical community should begin to collect past medical exposure information while they collect information on contact w/people who recently traveled to China:

1. Were you recently vaccinated using aluminum-containing vaccines?
2. Have you ever received a diagnosis of a SARS infection in the past?
3. Are you of Asian or Chinese descent?

With these three questions, we could learn a lot about the risk of mortality in a few weeks' time and plan an informed public health response accordingly.

Also, CDC and WHO should begin to inform owners of public businesses to have their staff wipe down commonly touched spots – door handles, light fixtures, bathroom fixtures, payment keypads, menus – and tell the public to use the Ebola "fist-bump" greeting. People should use their keys or a knuckle to push elevator doors.

These simple, low-cost cultural shifts will reduce the rate of spread of all virus-based disease, including influenza.

‹ Coronavirus Origins: Anatomy of a Scientific Inference

4 thoughts on “More on the ACE2-Related Asian COVID-19 Susceptibility Hypothesis”

Gary Haubold

February 16, 2020 at 9:39 pm

One of the most telling datapoints within China seems to be the higher mortality rate of male patients. What do you think accounts for the difference in mortality rates between adult males and females?

Higher rates of smoking in Chinese males is a leading candidate . . . .

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sissijanov (@janov3)

February 17, 2020 at 5:06 am

asian women suffer high rates of lung disease including cancer as they’ve switched to more western types of cooking oils..why do more boys suffer from autism and kawasaki..boys are subject to vaccine injury at a higher rate than girls..right wrong? can’t say smoking..might be..

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JB

February 17, 2020 at 4:50 pm

One has to wonder why this coronavirus is even newsworthy, when you consider the numbers on the 2 pages below, as well as the population of China vs the U.S.:

https://www.statista.com/statistics/1090007/china-confirmed-and-suspected-wuhan-coronavirus-cases-region/

Total of col. 2: 136,552
Total of col. 3: 3,509

Pop. of China ~1.4 billion
Pop. of U.S. ~330 million

https://www.cdc.gov/flu/about/burden/preliminary-in-season-estimates.htm
——
This is a massive marketing campaign…for God knows what. Given the vaccine research that you have published here, Dr. Weiler, a vaccine for this virus looks very difficult and perhaps undesirable.

So, what are we being sold?

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zyl
February 18, 2020 at 10:37 am

I think it would be better for you to say [I don't know].
Re ACE2, genomic variant by lab-work is already a popular tech, say, there are already patents.

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