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Coming to America: Genomic surveillance and how B.1.1.7 arrived in the US

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In this issue of Cell, Washington et al. and Alpert et al. demonstrate the value of genomic surveillance when studying the introduction of the B.1.1.7 variant to the US and illustrate the challenge that results from the lack of good sampling strategies.

In late 2020, scientists in the United Kingdom studying the SARS-CoV-2 pandemic noticed something unusual. In the southeast region of Kent, there was a sudden uptick in the number of samples of a particular lineage—separate infections without known links or shared exposures that nevertheless had extremely closely related genomes suggestive of being proximal infections in a relatively short transmission chain. Moreover, the mutations that defined the lineage included several that had been independently implicated in changing the properties of the virus for the worse (from a human perspective), here all together in one tidy package. Over the next few weeks, frantic efforts to define the characteristics of this “variant” confirmed that it was a serious event in the evolution of the pandemic, more transmissible and virulent, and we now know it as the “variant of concern” B.1.1.7 (Vozi et al., 2021). In this issue of Cell, two papers (Washington et al., 2021; Alpert et al., 2021) document and describe the introduction of B.1.1.7 to the United States, dating the first of multiple independent introductions to around Thanksgiving 2020. At the time of writing a few months later, B.1.1.7 is now the dominant lineage in the country and likely to be at least partially responsible for spiking infections from Michigan to Florida (CDC, 2021a).

Though both handle it cautiously and candidly, a common challenge for these two papers is that when B.1.1.7 was making landfall and becoming established in the US, genomic data from COVID cases in this country was very limited and efforts to collect it were unevenly distributed. Globally, it is hard to overstate how different the UK’s genomic surveillance program is from that of other nations, but the comparison with the US is instructive. As described in Alpert et al. (2021), for the 3-month period included in the paper (December 2020 to February 2021), only 0.43% of the US COVID cases were sequenced and deposited in public databases. In contrast, the sequencing effort that allowed the emergence of B.1.1.7 in Kent to be detected covered around 5% of all positive cases (Vavrek et al., 2021); in other words, around 10-fold more than the US.

Genomic surveillance is valuable, whether to detect variants or to infer or rule out transmission across scales (Figure 1A). But how can we manage national surveillance for an infectious disease when some places are not looking as hard as others? One possible workaround used by Washington et al. (2021) is to sequence a fraction of samples from commercial test providers. This is smart but imperfect as the resulting surveillance will be good in the places where that test is widely used and poor where it isn’t. Multiple cooperating commercial labs will do a lot to help this. Nevertheless, while sequencing truly random samples from commercial labs will provide a better estimate of the rise of known variants than an ad hoc alternative, or preferential sequencing of clusters of transmission (e.g., long-term care facilities), it is still not a substitute for a national strategy.

The challenge is not only to sequence more but to collect appropriate metadata, like date of sampling or epidemiologic and clinical features of infection, because without it, genomes are reduced to a much less useful string of Ts (and Ns). This, like sequencing, is easier said than done for a nation of diverse states with different attitudes toward an investment in public health (Maxmen, 2021).

Furthermore, the scientific community should also give fair credit to those who contribute sequence and other data to the public databases that make work of this sort possible. This is a truly valuable contribution that too often goes unrecognized and unrewarded by grant-making bodies and promotion committees. Researchers must be motivated to share data openly and in a timely fashion; perverse incentives that stand in the way of sharing data could literally cost lives.

It is the nature of things that during a pandemic of this kind, events overtake the patient collection of evidence and publication. This work documenting the introduction of B.1.1.7 to the US is being published when B.1.1.7 has already been acknowledged as the dominant lineage there. The significance is not limited to the findings of the papers but in demonstrating what can be done provided data are promptly available to inform policy and encourage future research. The issue of prompt reporting is shown clearly if we compare the lag time between samples being collected and submitted to the Global Initiative on Sharing All Influenza Data (GISAID, 2021) in the US and the UK (Figure 1B, median days of submission delay: 37 days in the US versus 19 days in the UK). Even had the US been sequencing as rigorously as the UK, such a lag in submissions would delay the detection of variants.

This is an ongoing concern. Lack of sampling strategies, limited sequencing, and delays in genomic surveillance...
continue to hinder detection of other emerging variants. B.1.1.7 has been joined by emerging variants of concern B.1.351 and P.1, the last responsible for a concerning surge of cases in a population thought to have high levels of prior immunity from previous infection (Sabino et al., 2021). Of these three, P.1 has recently been introduced to the US and is apparently rapidly becoming established in states including Illinois, Florida, and Massachusetts (CDC, 2021b).

Prompt reporting of genomic data is crucial to determining the epidemiological and clinical characteristics of this variant. Other variants continue to emerge. B.1.427/1.429 has recently been designated by CDC as “of concern,” and multiple lineages that are descended from or closely related to B.1.526 merit close attention (CDC, 2021b).

This is not only an issue for the United States. Recently screening revealed three travelers arriving from Tanzania into Angola infected with another “variant” that is more divergent than any yet reported (De Oliveira et al., 2021), showing how much might be happening in the peripheral vision beyond our current...
sampling frame. Surveillance might not seem the most exciting of topics, but it determines our ability to know almost anything about the status of the pandemic. This is reflected by the $1.7 billion investment in genomic epidemiology announced by the White House on the 16th of April (The White House, 2021), which will hopefully jumpstart programs across the country and mitigate the patchy sampling we have described here, even if it will take time and effort. Altogether, the work published in Washington et al. (2021) and Alpert et al. (2021) shows us how important it is to keep an eye on our adversary even, especially, as we deploy effective vaccines against it.

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Tracking self-performance in the prefrontal cortex: It’s layered

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In this issue of Cell, Spellman and colleagues record and manipulate the activity of neurons in the medial prefrontal cortex of mice performing a task in which they must pay attention to different stimuli. They show that this brain region is important for monitoring the animals’ performance, and neurons that appear to contribute to behavior reside in deep cortical layers.

An impressive but often effortless aspect of higher cognition is cognitive flexibility, or the ability to adjust our behavior depending on context. Cognitive flexibility, which is impaired in neuropsychiatric and neurodegenerative disorders, is often assessed using attentional set-shifting tasks (Brown & Tait, 2016). These tasks involve attending to a relevant stimulus over an irrelevant one to enhance processing of the relevant stimulus. For example, on an airplane, one might attend to their own music and tune out an announcement from the pilot. But if the plane encounters turbulence, one may switch their attention to the pilot’s message. Similarly, in attentional set-shifting tasks, subjects are required to exhibit a response based on a relevant stimulus while ignoring an irrelevant one. Following a rule change, the subject must shift their response to depend on the previously irrelevant stimulus. Rule changes are often uncued and must be inferred by...