Communication

Addressing the Concerns Surrounding the Recent Outbreak of SARS-CoV-2 Subvariant BA.2.86 (Pirola)

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Addressing the Concerns Surrounding the Recent Outbreak of SARS-CoV-2 Subvariant BA.2.86 (Pirola)

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Abstract: The emergence of SARS-CoV-2 subvariant BA.2.86, also known as Pirola, has raised concerns about its transmissibility, virulence, and immune escape. The aim of this letter is to address the current evidence on the origin, spread, and characteristics of Pirola, and discuss its implications for public health and vaccine development. The need for enhanced surveillance, genomic sequencing, and epidemiological studies to monitor the evolution and impact of Pirola and other SARS-CoV-2 variants are highlighted in this letter along with the importance of global cooperation and coordination to prevent and control future outbreaks of this novel coronavirus strain.

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Dear Editor,

In recent developments, a novel SARS-CoV-2 subvariant, designated as BA.2.86 and colloquially referred to as "Pirola," has garnered significant attention within the scientific community. This variant has surfaced in multiple countries, including Denmark, Israel, the UK, and the US, raising substantial concerns due to its distinctive genetic makeup characterized by an unusually high number of mutations [1,2]. BA.2.86 has 36 spike amino acid mutations relative to variant XBB.1.5 and 38 such changes compared with variant EG.5.1, suggesting evolutionary adaptation under strong antibody pressure. It has exhibited potential abilities to evade immune responses, particularly neutralizing antibodies, which are vital components of the body's defense against viral infections [1]. Genetic sequencing has identified BA.2.86 in six confirmed COVID-19 cases, dating back to its earliest detection in Denmark on July 24th. Notably, these cases appear unrelated, suggesting community transmission. Genetic diversity analysis indicates that BA.2.86 has been circulating for several months. Intriguingly, all of its more than 30 mutations are located within the spike protein, which endows BA.2.86 with characteristics indicative of potential heightened transmissibility, cellular entry and immune evasion. Some of the mutations, such as N501Y, E484K, and K417N, are located in the receptor-binding domain (RBD), which directly interacts with ACE2. These mutations increase the affinity and stability of the RBD-ACE2 complex, enhancing the viral infectivity. Other mutations, such as L452R, Y144del, and H69del, are located in the N-terminal domain (NTD), which is involved in immune evasion. This extensive mutational profile sets BA.2.86 apart from its predecessors, including BA.2 and XBB.1.5.

While the number of BA.2.86 sequences was limited, they are originated from various countries, suggesting potential global transmission. It's uncertain whether BA.2.86 will follow the path of most new variants, which typically do not spread widely, or if it possesses the traits for broader dissemination, similar to the original Omicron or XBB variants. Insufficient data hinders confident predictions [3]. Deep mutational scanning suggests that it is likely to exhibit equal or greater antibody escape than XBB.1.5, the strain used for fall vaccines. Additionally, it presents antigenic mutations relative to XBB.1.5, potentially conferring further advantages. For BA.2.86 to succeed, it must combine its antigenic edge with transmissibility comparable to current XBB variants. However, accurate transmissibility assessment remains challenging due to the current lack of data. Early assessments

conducted by Dr. Jesse Bloom of Fred Hutchinson Cancer Center, reveal that BA.2.86 demonstrates at least a comparable degree of antibody escape as XBB.1.5 when compared to BA.2 [3]. The World Health Organization has designated BA.2.86 as a "variant under monitoring" on August 2023, placing it in the second tier of notable COVID-19 variants.

Current knowledge on the transmissibility and disease severity associated with BA.2.86 remains limited. However, scientists anticipate that its transmissibility may not significantly differ from other circulating omicron strains. This expectation stems from the recognition that multiple mechanisms of immunity, beyond neutralizing antibodies, offer protection against severe disease, thanks to the widespread vaccination and prior infections [1]. While concerns about its impact on public health persist, experts believe that even in a worst-case scenario, it is unlikely to result in a resurgence of severe disease comparable to earlier pandemic phases dominated by alpha, delta, or omicron variants. The emergence of BA.2.86 may be linked to a long-term infection in an immunocompromised individual over a year ago, followed by its introduction into the broader community [1]. This subvariant has likely circulated undetected in regions with limited viral surveillance and subsequently spread globally. Ongoing monitoring will elucidate its performance relative to other omicron subvariants in the weeks ahead.

BA.2.86 has made its presence known in various countries, including Canada, Israel, Portugal, South Africa, Sweden, the UK, and the US [4]. Concerningly, the UK has reported cases in care homes, with the UK Health Security Agency detecting a cluster of 28 cases within a Norfolk care home [5,6]. Despite the rising numbers, it remains uncertain if BA.2.86 will exhibit altered clinical severity or become the predominant variant in the UK. Given the emergence of BA.2.86, public health agencies are closely monitoring the situation. In response to the potential threat, England has expedited the rollout of the autumn vaccine booster as a precautionary measure. The US has also observed cases, prompting the Centers for Disease Control and Prevention (CDC) to investigate further, though they emphasize that current COVID-19 trends are not primarily driven by BA.2.86 [5]. Preliminary evidence from the National Wastewater Surveillance System (NWSS) in the US suggests the presence of BA.2.86 in wastewater samples. Continued monitoring of wastewater will provide valuable insights into the prevalence and spread of this variant.

BA.2.86's genomic makeup distinguishes it from prior omicron variants, potentially challenging existing immunity derived from vaccines and previous infections. While laboratory testing of antibodies remains limited, the existing population-wide immunity is expected to offer some level of protection against severe disease. Research in this area is ongoing. Analysis of BA.2.86's mutation profile indicates that current treatments such as Paxlovid, Veklury, and Lagevrio should remain effective. The impact on molecular and antigen-based diagnostics is anticipated to be minimal. The emergence of the BA.2.86 subvariant underscores the dynamic nature of the SARS-CoV-2 virus. Vigilant monitoring, research, and public health measures are essential to navigate the evolving landscape of COVID-19 variants. While concerns persist, the scientific community remains cautiously optimistic, emphasizing that existing immunity and therapeutic options offer some degree of protection against the potential challenges posed by BA.2.86. Continued research will provide critical insights into the variant's behavior and its implications for public health.

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