The unsung virtue of thermostability

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The current vaccination campaign against SARS-CoV-2 has many challenging aspects, one of which is maintaining the cold chain for the distribution, delivery, and storage of available vaccines and guaranteeing that their full titre is retained for administration. Although outstanding technology for vaccine development has enabled products to be put on the market in 1 year, it is difficult to understand why approximately the same length of time is taken to roll out their administration, thus jeopardising the effect of the campaign. Additionally, if a substantial proportion of vaccines lose their potency or safety, or both, because of problems during transportation and storage, they will be less efficacious, and an increase in the overall costs of deploying the campaign will be inevitable. The reason for having to implement the cold chain is that thermostable vaccines do not exist (ie, heat-stable and freeze-stable, so as to be stored at a temperature of >8°C, which is a preferred vaccine characteristic recommended by WHO).[1] No COVID-19 vaccine exists in a format that could be delivered to homes by mail and, ideally, self-administered.

In actuality, high-income countries were not really interested in and committed to developing thermostable vaccines, because this feature was never expected to become a major hurdle in the limited scope of scientists. There was a failure to identify any foreseeable circumstances under which high-income countries would not have enough refrigerating capacity to manage any widespread vaccination campaign. For this reason, developing thermostable vaccines was never a priority or a core requirement for high-income countries. In fact, the real demand and insufficient push for thermostable vaccines, both in veterinary and in human medicine, comes from low-income and middle-income countries and, although supported by international organisations, it was never prioritised to become an essential characteristic sought by vaccine developers, industries, and funding entities.

Perhaps investing in global needs, which include the needs of the poorest people, would have benefited the whole of humanity in tackling the COVID-19 pandemic. Now is the time to reprioritise the urgent improvements in vaccine development that are essential to fully make use of the power of immunisation campaigns even under diverse epidemiological, geographical, and logistical circumstances.

We declare no competing interests.

Ilaria Capua, Carlo Giaquinto
icapua@ufl.edu

One Health Center of Excellence, University of Florida, Gainesville, FL 32611, USA (IC); University of Padua, Padua, Italy (CG)

1 WHO. Assessing the programmatic suitability of vaccine candidates for WHO prequalification. Geneva: World Health Organization, 2012.

Rapid identification and tracking of SARS-CoV-2 variants of concern

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In the past few months, we have seen emergence of clinically important mutations that alter infectivity, severity, or immune susceptibility of SARS-CoV-2.[1] Prominent examples include Asn501Tyr, His69_Val70del, and Glu484Lys mutations in the spike protein that have emerged independently in many global strains, such as those from the UK, South Africa, and Brazil, possibly driving resurgence of the pandemic when it appeared to be coming under control.[2] Some of these variants are likely to be resistant to vaccines and capable of reinfections. Future public health policy and pandemic response will need knowledge of the presence of such variants in the local population and their rapid identification on introduction into communities. This is not possible without local sequencing capacity, which is scarce in many vulnerable parts of the globe, where lockdown regulations are not strictly enforced and movement is unrestricted.[3] Even in those low-income and middle-income countries where such capacity is present and high alert is in place, the delay between positive diagnosis and sequencing results leads to an opportunity for a new variant to become established. Hard quarantine, involving strict confinement and isolation for all people with a positive test for SARS-CoV-2 who are at risk of carrying clinically important new variants, until cleared by sequencing, is a public health measure that is difficult to implement. This difficulty arises because long turnaround times that are associated with sequencing might lead to extra pressure on healthcare authorities for institutional quarantine or follow-up after release in the event of variant detection in an individual. Diagnostic platforms that are based on sequencing and are suitable for use at the point of care, such as pore-based technologies, are anticipated to contribute substantially to this process in the near future, being capable of diagnosis, variant calling, genealogy, and novel mutant detection. Until then, we propose an alternative approach for low-resolution, yet accurate, early detection of specific variants of concern through clustered interspaced short palindromic repeats (CRISPR) diagnostics, which rely on the specific DNA interrogation properties of enzymes, such as FnCas9, Cas12, or Cas13, to identify variants of concern through fluorescence or paper strip-based diagnosis (appendix).[4] Such tests are rapid, inexpensive, and especially suited for low-income countries. Even where sequencing is being done, CRISPR diagnostics can help to isolate variants in the first instance, which can then be sequenced to validate and map coexisting mutations (appendix). We have used this approach to identify the Asn501Tyr variant of concern, starting

See Online for appendix