Public comments for the coming NSABB meeting

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Proposals for future governance of GOF research of the kind that creates ePPPs

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GOF studies of the kind that create ePPPs have focused on avian influenza viruses, SARS viruses and MERS viruses. A common feature of these pathogens is that they tend to cause aerosol-mediated respiratory tract infections and have the potential to be readily transmitted to non-immune populations. Thus, intentional mutation of pathogens derived from animal hosts to induce properties that make them infectious to humans makes them capable of causing pandemics.

Many emerging infectious diseases are caused by mutations in pathogens that originally infect animals and jump the species barrier to become infectious and contagious to humans. So far, the main objectives of GOF research to create ePPPs have been (1) to elucidate the mechanisms that lead to the transmission from animals to humans, (2) to contribute to the anticipation and surveillance of predictions of outbreaks such as endemics and pandemics, and (3) to select suitable vaccine strains. On the other hand, since ePPPs are artificially created through research, there is a risk of inadvertent leakage or intentional misuse that could lead to a pandemic. This is the most worrisome aspect of such studies, and the feasibility of conducting any particular study should be considered after a thorough examination of the balance between risks and benefits.

However, a review and analysis of the results of GOF research to date indicates that the

benefits to society are limited. In other words, the benefits have not been sufficiently proven to significantly outweigh the risks, but there is a minority view that the benefits will clearly outweigh the risks in the future[Ref]. (1) As for the mechanism of jumping the species barrier, which is shown above as the so-called "advantage of GOF research to create ePPPs," simulations based on computer models and specific analysis of genes in the relevant area are expected to produce sufficient information, and the advantage of daring to create ePPPs has not been proven. Therefore, the merit of creating ePPPs has not been convincingly demonstrated. In addition, (2) as for epidemic forecasting and surveillance, there is no evidence showing that ePPPs have contributed to the clarification of actual epidemics. As the most important benefits of scientific and technological progress in this respect are the rapid and mass sequencing of genomes and the advancement of their analysis systems, it is difficult to believe that the merits of GOF research outweigh these benefits. (3) When it comes to the selection of vaccine strains, it is nearly impossible to predict in advance, as pathogens can mutate rapidly. Even if the prevalent pathogen strain could be identified in advance, that itself cannot be used immediately as a vaccine as its efficacy can only be proven in actual clinical studies in the late stage. Therefore, as shown in our experience of COVID-19, the useful vaccine development technologies are (1) mRNA development technology, (2) recombinant virus vector technology, and (3) creation of inactivated vaccines based on epidemic strains, and there is very little evidence to justify the significance of creating ePPPs.

Taken together, we believe that there is little scientific evidence that the benefits outweighed the risks in GOF studies to create ePPPs. Therefore, the advantage of continuing such studies in the future seems very low. We also believe that continuing such studies is an inappropriate choice from the perspective of avoiding the associated risks.

Of course, we are clearly against restricting the freedom of scientific research and legitimate research based on the spontaneous ideas and intentions of researchers. It is desirable that science and technology be developed in a sound manner and applied in a way that contributes to society. From this standpoint, we believe that what should be promoted should be promoted, and that measures should be taken to ensure that the studies that are needed are properly governed.

Based on the above, we propose the following:

1. Establish a moratorium on GOF research that produces ePPPs for the time being, and consider banning research unless the significance of the research that should be conducted is well demonstrated.
2. For research involving the risk of infection, including GOF research to create ePPPs, the same measures should be taken regardless of whether the research is conducted or funded by a public or private institution.
3. Research using specific pathogens, regardless of whether it is GOF research to create ePPPs or not, carries risks. Therefore, - transparency and traceability should be ensured in the conduct of the research, while biosafety/biosecurity is adequately ensured.

Researchers and research facilities should be open to disclosure of all information as long as it does not interfere with patentability and originality of the research.

Our position on the GOF study to create the ePPP is as stated above, but we are sure that there are those who disagree with this position, and we sincerely hope that both sides can reach a common conclusion after a frank discussion in order to deal with this issue in the future. We are convinced that such open debate is the best way to ensure the future of necessary research and its effective management.

It is our sincere hope that the NSABB meeting will take the above proposals into full consideration, and that the discussions will proceed appropriately and result in a meaningful conclusion.

Reference

Shinomiya N, Minari J, Yoshizawa G, Dando M, Shang L. Reconsidering the need for gain-of-function research on enhanced potential pandemic pathogens in the post-COVID-19 era. Front Bioeng Biotechnol. 2022 Aug 26;10:966586. doi: 10.3389/fbioe.2022.966586. PMID: 36091454; PMCID: PMC9458934.