GAIN-OF-FUNCTION

What is “Gain Of Function” (GoF) research?

Gain-of-function research is medical research that genetically alters an organism in a way that may enhance the biological functions of gene products. This may include an altered pathogenesis, transmissibility, or host range, i.e. the types of hosts that a microorganism can infect.

In virology, GoF research is usually carried out to better understand current and future pandemics.

The term "gain of function" is sometimes applied more narrowly to refer to research which could enable a pandemic-potential pathogen to replicate more quickly or cause more harm in humans or other closely-related mammals.

Is this research dangerous?

Some forms of GoF research carry inherent biosafety and biosecurity risks, and are thus also referred to as dual use research of concern (research which might easily be misapplied to do harm).

Significant debate has taken place in the scientific community on how to assess risk-benefit of GoF research, and how to engage the public in deliberations for policymaking.

What are the concerns?

Biosafety, relating to the accidental release of a pathogen into the population, biosecurity relating to the intentional release of a pathogen into the population, and bioethics, the principles of biorisk management and research review procedures.

What are the 7 experiments of concern that should not be pursued if they could create pathogens that are not already present in nature?

1. Demonstrating how to make a vaccine ineffective
2. Developing a pathogen's resistance to antibiotics or antiviral agents
3. Enhancing a pathogen's lethality or making a non-lethal microbe lethal
4. Increasing the transmissibility of a pathogen (e.g. making a non-airborne pathogen airborne)
5. Altering the host range of a pathogen by increasing the number of species it can infect
6. Enabling a pathogen to evade diagnostic testing
7. Enabling a biological agent or toxin to be weaponized

Any examples?

Some GoF research creates viruses with abilities they do not have in nature.

In 2011, scientists famously and controversially did just that with bird flu, resulting in a version capable of airborne transmission among ferrets. The naturally occurring virus does not have this ability. Making mammal-to-mammal transmission easier.

In 2015 researchers engineered a hybrid pathogen that combined features of the original SARS virus (SARS-CoV) that infected humans in the early 2000s with that of a bat coronavirus. The result was a pathogen that could enter human cells and also cause disease in mice. As demonstrated by experts quoted in a 2015 article in Nature: one said that all the research did was create a "new, non-natural risk" among the multitude that already exist, while another contended that it showed the potential for this bat virus to become a "clear and present danger".

Is there evidence of Covid-19 Gain Of Function Research?

A group of virologists at Boston University did the following. They took the spike protein from the Omicron strain of SARS-CoV-2 and combined it with an early 2020 strain of the Covid-19 virus.
This experiment gave them a brand-new, never-before-seen strain of Covid-19. Was it more deadly? Absolutely.

In their experiments, the BU scientists infected laboratory mice with the original Omicron virus, which caused "mild, non-fatal infection" but when they infected mice with their new, recombinant virus, which they called Omi-S, 80% of the mice died. To quote from their article:
"the Omicron S-carrying virus inflicts severe disease with a mortality rate of 80%".

Alternatives to gain of function research?

Researchers can test the capacity of virus proteins to engage with different kinds of cells. Software can predict how these proteins might interact with various cell types or how their genetic sequences could be associated with specific virus features. Also, if the researchers use cells in a lab dish, the viruses might be designed not to replicate.

Another option is loss-of-function research. Using versions of a virus with less pathogenic potential is another way to unlock that microbe's secrets. Still, highly pathogenic forms can be quite different from their less threatening counterparts—for example, they may differ in how often they replicate—possibly limiting the usefulness of such studies.

Is this work so valuable for public health that it overshadows the risk to public health in doing it?