

# Gain-of-function research

Gain-of-function (GoF) experiments aim to increase the virulence and/or transmissibility of pathogens, in order to better understand them and inform public health preparedness efforts.<sup>[104]</sup> This includes targeted genetic modification (to create hybrid viruses), the serial passaging of a virus through a host animal (to generate adaptive mutations), and targeted mutagenesis (to introduce mutations).<sup>[105]</sup> Lipkin is a listed “supporter” of GoF advocate group, *Scientists for Science*,<sup>[106]</sup> which was co-founded by Columbia colleague Vincent Racaniello.<sup>[107]</sup> The US National Institutes of Health placed a moratorium on GoF research in October 2014, and lifted the moratorium in December 2017, after the implementation of stricter controls.<sup>[108][109]</sup>

## Lipkin's views

Lipkin, while not endorsing every GoF experiment, has said that “[t]here clearly are going to be instances where gain-of-function research is necessary and appropriate.” In the example of Ebola, which is incapable of airborne transfer, Lipkin believes that “researchers could make a case for the need to determine how the virus could evolve in nature by engineering a more dangerous version in the lab.” Lipkin believes that there should be guidelines in place to govern GoF experiments.<sup>[110]</sup>

Regarding the security level of labs in which work on dangerous pathogens can be performed, Lipkin noted, “(w)ork is more expensive and less efficient when pursued at biosafety level 4 (BSL-4) than at BSL-3 or... BSL-3-Ag (agriculture).” Whereas BSL-4 requires facilities to be inspected daily, personnel to be monitored for symptoms of disease, and virus samples, equipment, and personnel to be logged in and out, Lipkin noted: “These measures are not required at BSL-3”.<sup>[111]</sup> He said BSL-3 labs (such as the ones at Columbia and Sun Yat-sen University,<sup>[112]</sup> with which Lipkin and Columbia collaborate<sup>[113]</sup>), should be allowed to conduct GoP work on globally active viruses in order to expedite research for a vaccine, though he added “there should be some sort of guidelines”.<sup>[114]</sup>

To illustrate his stance, Lipkin referenced *Contagion*, where the maverick scientist (played by Elliot Gould), conflicts with health authorities, a story which was “loosely based on my experiences during the West Nile Virus outbreak in 1999.” In the movie, the researcher is told to “cook his samples” and that all research is to be moved to the BSL-4 lab due to security concerns, but he “ultimately find(s) a way to grow the virus and make a vaccine” and save the world. In real life, Lipkin recounted: “Although our team identified the causative agent (WNV), political wrangling delayed permitting and shipment of the virus to our laboratory. To expedite diagnostics and drug development, I decided to recover the virus by transfecting genomic viral RNA.”<sup>[114]</sup> Unlike the movie, no effective vaccine for humans was found for West Nile Virus,<sup>[115]</sup> as a result of GoF research.<sup>[116]</sup>

# Criticism of GoF

Ian Mackay (University of Queensland, Australia), said: “One cannot legislate for every accident or human error; all manner of things can go wrong, and if an outbreak spreads to the community the consequences could be horrendous.”<sup>[109]</sup> Marc Lipsitch (Harvard University, MA, USA) argued that GoF research is dangerous and unnecessary, saying that deliberate mutations of viruses have not produced novel insights. “There is nothing for the purposes of surveillance that we did not already know. Enhancing potential pandemic pathogens in this manner is simply not worth the risk.”<sup>[109]</sup> According to a Lancet article, the moratorium on GoP was prompted by a slew of accidents in the US at BSL facilities in 2014: “The news that dozens of workers at the Centers for Disease Control and Prevention (CDC) might have been exposed to anthrax, that vials of smallpox virus had been left lying around in an NIH storeroom, and that the CDC had unwittingly sent out samples of ordinary influenza virus contaminated with H5N1, shook faith in the country's biosafety procedures.”<sup>[109]</sup> Funding for GoP research in the US resumed in 2017.<sup>[117]</sup>

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