AMERICAN SOCIETY FOR MICROBIOLOGY

Gain of Function Research

What is Gain of Function Research?

Gain of function is a broad term that can encompass almost any type of research aimed at understanding mechanisms and processes. Gain of function techniques are used in research to alter the function of an organism in such a way that it is able to do more than it used to do. (The inverse process in research is referred to as "loss of function.") This may be accomplished in the lab by adding to or changing the organism's genetic sequence, and this type of research has had a positive impact on basic and applied life science research.

Why Do Scientists Use Gain of Function Techniques in Research?

Outside of the lab, where microbes are facilitated by only natural selection in their respective environments, gain of function is a naturally occurring evolutionary process. In fact, microorganisms accumulate mutations in their genomes almost every time they divide. For example, antibiotic resistance is often acquired when bacteria gain and incorporate entire plasmids into their genomes. The process is further demonstrated by the continued emergence of SARS-CoV-2 variants.

But the natural process of gain of function occurs too slowly for scientists to study, so the gain of function technique is employed to develop better experimental tools to advance scientific discovery, understand the natural processes that are occurring, and develop solutions to medical conditions or other problems in the living world around us.

How Have We Used Gain of Function in Life Science Research?

Gain of function techniques have contributed to lifesaving developments in medicine and also in developing practical solutions in other areas of society. For example, these techniques have led to basic microbial science discoveries and advances in genetics, as well as to translational and clinical advances such as new therapies for cancer and for cystic fibrosis. Gain of function research techniques have been used to develop vaccines against infectious diseases including Johnson & Johnson's COVID-19 vaccine. It also has been used in insulin production for people with diabetes. Benefits are not limited to the field of medicine. These techniques have also been used to address agricultural challenges such as crop resiliency and crop yield.

What Are the Concerns Associated With Gain of Function Research?

Certain types of gain of function research -- for example, Gain of Function Research of Concern, Dual Use Research of Concern or Enhanced Potential Pandemic Pathogen (E3P) -- raise important biosafety and/or biosecurity concerns. While these are an extremely small subset of gain of function experiments (estimated at less than 1 percent), they require a higher level of review and are subject to strict protocols.

Policies at the institutional, state, federal and global levels help ensure that this research is conducted ethically, safely and securely by trained professionals at facilities that comply with strict physical containment procedures.

- **Review and Approval Processes** - All research must be subjected to review and obtain institutional and federal approval before funding is allocated and/or experimentation begins.
- **Physical Containment** - Laboratories must follow and undergo regular inspection to prove that they are in compliance with the CDC's physical containment guidelines (see biosafety levels below). They must demonstrate that personnel are properly protected, safety guidelines are in place, equipment is operational and organisms are properly contained within the lab.
- **Intensive Training and Background Checks** - Anyone working on high-risk research projects goes through lengthy and intensive, hands-on laboratory training. This includes everyone from scientists to laboratory technicians. They also in some cases must submit to background checks by the FBI to be permitted to work with certain pathogens.
- **Procedural Monitoring** - Procedural competencies are regularly monitored through annual training, pop quizzes, FDI background checks, CDC approvals/checks, etc.

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What Are the Different Biosafety Levels for Labs Conducting This Kind of Research?