Gain of Function Research

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What is Gain of Function Research?

Gain of function research is a term that refers to techniques 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, and to understand how this occurs in the environment. (The inverse process in research is referred to as "loss of function.") Gain of function occurs naturally as viruses and other microbes evolve and may also 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 zoonotic diseases like avian and swine influenza.

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.

What Are the Concerns with Gain of Function Research, and How Are They Mitigated?

Certain types of gain of function research — for example, Gain of Function Research of Concern, Dual Use Research of Concern or Pathogens with Enhanced Pandemic Potential (PEPP) — raise important biosafety and/or biosecurity concerns. While these are an extremely small subset of gain of function experiments, they require a higher level of review and are subject to strict protocols.

Policies at the institutional, state, federal and global levels ensure that this research is conducted ethically, safely and securely by trained professionals at facilities that comply with strict physical containment procedures. However, sufficient funding and staffing are needed to ensure full compliance.

- **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 adhere to strict processes and undergo regular inspection to prove that they are in compliance with the CDC's physical containment guidelines. 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** - Everyone working on high-risk research projects goes through lengthy and intensive, hands-on laboratory training. 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, CDC approvals/checks and lab safety inspections.

How is Gain of Function Research Regulated?

Gain of function research is covered by federal biosafety and biosecurity research regulations, including policies and frameworks covering Dual Use Research of Concern (DURC) and research with Pathogens with Enhanced Pandemic Potential (PEPP). For more information on these regulations, see the Administration for Strategic Preparedness and Response Science, Safety and Security website.

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

Gain of function research is a powerful tool in the laboratory that has resulted in developments that positively impact human, agricultural and environmental health. These include the development of cancer therapeutics, bioremediation and the engineering of drought- or pest-resistant crops.

Examples:

- **Chronic Disease:** New therapies for cancer, cystic fibrosis, diabetes and cardiac pacemaker repair.
- **Infectious Disease:** Vaccine development including coronavirus and dengue fever vaccines.
- **Agriculture:** Developing treatments for bacterial infections affecting crops, increasing crop resiliency, crop yield, pest mitigation and animal health.

Source: https://journals.asm.org/doi/10.1128/mbio.00188-23

Policy Recommendations:

Standardize Research Terminology and Practices

- Clearly define terms like "gain of function" to ensure a common understanding of which categories of gain of function research require enhanced scrutiny.
- Standardize biorisk management protocols and practices, both in the U.S. and internationally. Support the sharing of best practices to help develop standard biocontainment and biosafety protocols.

Increase Transparency and Public Engagement

- Facilitate open dialogue about the risks, benefits and safety measures to build public confidence and inform policy decisions.
- Require the inclusion of virologists, public health experts, environmental microbiologists and biosafety experts on boards or committees established by Congress or the Executive branch to oversee life sciences research.

Strengthen Safety Systems

- Increase funding for biosafety measures, training, improved facilities and personal protective equipment.
- Standardize reporting systems for lab accidents, including anonymous reporting and constructive responses, to enhance data collection and inform risk-benefit analyses.

For more background on Gain of Function, visit https://asm.org/reports/impact-assessment-of-research-on-infectious-agents.