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Biohackers

A growing number of amateurs join the do-it-yourself molecular biology movement outside academic laboratories

Karl Gruber

Just a bit more than a decade ago, genetic engineering was the sole purview of biologists with an advanced degree working in highly specialized laboratories. PCR, for instance, a staple technique of molecular biology to create multiple copies of DNA fragments, requires DNA synthesizers, PCR machines, and reagents that used to be expensive and were only available to researchers working in academic or industry laboratories. Today, anyone wanting to dwell into molecular biology can buy a PCR machine, reagents, primers, and other materials online. The same is true for cloning experiments: Anyone with Internet access can easily find protocols online and order DNA sequences, reagents, and equipment. Amateur molecular biologists can even save themselves from the hassle of buying equipment and reagents, and join a community laboratory to run their experiments. As a result, more and more people are becoming do-it-yourself (DIY) biologists or biohackers, amateurs outside traditional academia, who tweak DNA, as well as any trained researcher, but without having to submit to the rules of mainstream science.

The biohacking world

To some, biohackers are just a group of wannabe scientists, while others think they are a creative force to some extent akin to the computer hackers in the 1990s who started a whole new industry. However, some are worried about the potential safety and health risks of DIY biohacking. These concerns relate not only to nefarious or criminal abuse to create biological weapons or modify pathogens, but also to human and public health. These worries are not at all unfounded. Indeed, there are examples of amateurs trying to circumvent the usual route and safety checks of clinical research, such as a biohacker who tried to develop a purported cure for lactose intolerance [1]. Skipping the traditional routes of human clinical trials, he swallowed his concoction during a live web stream. Similar stunts can be found for DIY approaches developed by biohackers to treat anything from herpes and HIV to increasing your muscle mass [2,3].

Outside the academic realm

But not all biohackers follow this path. Meet Keoni Gandall, who performed his first cloning experiment while in 7th grade, at age 12. Today, he is heading his own research project at Stanford University—all without a formal training or degree in science. For Keoni, it started with a book and his biology teacher. "Back in 6th grade, I found a virology textbook at the local church book fair. I thought, 'Huh, this is pretty cool', and began reading it. It took me a while to get through the first chapter, but I learned a lot about molecular bio, and I continued reading about it. In 7th grade, my bio teacher saw that I was really into biology, so he let me order a bacterial transformation kit to his classroom for me to do at home. After I did that, I was hooked", he recalled.

Since then, Keoni has gone a long way into the nuts and bolts of biotechnology. At age 19, he has gathered more knowledge than the average biologist. "I can basically engineer micro-organisms well. I know techniques for several bacteria, yeast, phage, etc., as well as most, if not all, the current popular DNA cloning techniques", Keoni said. "I work at a pretty high level and make robots do most of the actual work, so mostly what I do is engineer software for the design of DNA, the operating of the robots, and the management of our databases".

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Today, Keoni is working for the BioBricks Foundation at Stanford University (biobricks.org) and leads the Free Genes project, to make DNA biotechnology more accessible to the general public. In essence, Free Genes will synthesize and deliver genes for anyone and keep a copy for itself. Keoni was hired by Drew Endy, President of the BioBricks Foundation and Professor at Stanford University. "We hired him because we were excited about his research experiences and research perspective, both of which we concluded as very impressive and full of potential", Endy explained. The fact that Keoni was not part of an academic career structure was another factor. "Most postdocs feel the need to rapidly complete several high profile projects and get snazzy papers in scientific tabloids so that they can convince administrative bodies to give then faculty/PI positions", Endy explained. "The Free Genes project is not well suited for such work. Stated differently, staffing biology projects only from the perspective of traditional academic or traditional for-profit organizations limits the type of biology that can be accomplished".

At 19, and despite his experience, Keoni has no plans to go to college. "What value

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would it add to my life, and what would the opportunity cost be? Seeing my friends go through it, it doesn't seem very attractive: high levels of stress, midterms on things that will later be completely useless to me, and being forced to take classes you don't care about. All for a piece of paper at the end of it", he said. "I'd rather learn from a network of brilliant people who care about what they're doing. I'm not going to pay someone to make my life hell for 4 years to just get a slip of paper at the end of all of it". Instead, Keoni pursues his idea of creating life. "I dream of a day when we can design life from scratch", he explained. "I want to sit down at a computer and be able to design a life form completely unknown to this world and be able to bring it alive from chemicals within a matter of days/weeks".

Bringing biology to the masses

Undoubtedly, a good aspect of the biohacking movement is making molecular biology more accessible to a wider range of people, most of whom are outside the academic realm, to learn and practice high-end biological techniques. "I think the good thing about biohacking is that it is enabling a type of active scientific literacy that has been long missing from the modern life sciences and biotechnology", Endy said. However, he pointed out that while biohacking can be seen as a positive movement, it is still a long way from having a significant impact, especially when compared to the rise of amateur electronics and computing in the 1970s. "The tools and technologies needed to make biohacking practically effective for everyone do not now exist. The situation is very much *not* like the state of electronics and computing in the 1970s when the Homebrew Computer clubs got going and contributed to/helped lead the development of the personal computer", Endy commented.

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In addition, there are obvious risks in pursuing some biotechnological endeavors outside academic realms. Many things can go wrong, even with the best intentions at heart, noted Marcus Graf, chair of the board at the International Gene Synthesis Consortium (IGSC), an international industry-led group that represents nearly 80% of the world's gene synthesis companies. He argues that the involvement of academia is vital to ensure biohacking does not end up with unfortunate outcomes: Academic institutions could provide space within their laboratories to teach amateurs about gene editing and other technologies. In the process, enthusiasts would learn about the risks and the hurdles of cloning or gene editing, in particular, when it involves the human body.

Such approaches have already been deployed with initiatives such as the International Genetically Engineered Machine (iGEM; igem.org) competition or Genspace. iGEM is a non-profit organization that promotes the understanding of synthetic biology through competitions. It began as a synthetic biology course at the Massachusetts Institute of Technology (MIT) in 2003 and developed into a competition the following year, with five teams participating. In 2017, more than 300 teams from 40 countries took part. The competition is not just for fun: So far, more than 30 start-up companies have resulted from projects presented at iGEM. Participants, usually undergraduate students, have to follow a strict set of safety guidelines and regulations. These include laboratory safety practices or regulations about the use of dangerous organisms like pathogens.

Genspace, founded by tech journalist turned biohacker Daniel Grushkin and biologist Ellen Jorgensen, can be thought of as a kind of community garden. It is a fully equipped public laboratory that anyone can use to do experiments. (www.genspace.org) Membership fees range from US$250 per month to join the laboratory to US$800 to have your own desk and bring up to two people to help with experiments. Genspace also offers introductory courses, such as the Biohacker Boot Camp or the Biotech Crash Course. "More than 6,000 people have taken our classes since 2012, in topics ranging from biotechnology basics, microbiology, CRISPR-Cas9, neuroscience, personal genetics, bioart and biodesign, and more", commented Beth Tuck, Director of Science Education at Genspace. "80% do not have a traditional life sciences background (i.e undergraduate or graduate training), and there is a fairly even split between people coming from computer science and engineering, art and design, and curious adults and teachers".

> *"... while anyone can, in theory, order a string of DNA online, there are strict regulations in place to prevent people ordering..."*

It has also produced start-ups like Opentrons, which makes open-source liquid-handling robots, and research collaborations, such as the BK Bioreactor Project, which described the microbiome of the Gowanus Canal in New York City. Even art has spawned from Genspace, like the Stranger Visions Project, which used hairs, chewed up gum, and cigarette butts found in streets, public bathrooms, and waiting rooms of New York City to extract DNA samples and reconstruct the face of the owner of these trivial objects.

Another good example of DIY science led by the masses is Foldit. On 2017, the candy maker Mars, Thermo Fisher Scientific, and other partners, including many from academia, created the Foldit platform, which allows anyone to participate in a research project aimed at elucidating optimal enzyme structural conformations (https://fold.it/portal). It takes the form of an online game where players would tweak an enzyme structure with the goal of finding a more optimal conformation, which, ideally, would lead to an optimal function of the enzyme. Their first goal was to design an enzyme against aflatoxin, a dangerous food toxin. The platform now hosts more than 50,000 players who tackle different problems in protein folding.

While Foldit has been a great success, the question remains whether such approaches are feasible in scientific fields such as gene editing. It would need a more serious commitment of time and money from scientists and laboratory space open to anyone. But there are also potential problems that could arise from a wider and uncontrolled use of DNA technology by amateurs.

Security concerns

One long-standing fear is that a biohacker could use the technology for nefarious

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purposes: like creating a highly contagious virus or a dangerous toxin for terrorist or criminal activities. The technology needed to create a virus already exists, and anyone who knows the biotech arena can even have some of the work done online. In January 2018, a group of Canadian and American scientists stitched together DNA fragments to create a live (and infectious) horsepox virus [4], an extinct relative of the well-known smallpox virus. All the sequences were ordered by mail from DNA synthesis companies.

However, while anyone can, in theory, order a string of DNA online, there are strict regulations in place to prevent people ordering, for instance, a toxin gene, or a gene from a dangerous virus. The International Gene Synthesis Consortium monitors all incoming orders of DNA sequences larger than 200 bases to ensure that orders meet a minimum safety standard and to prevent the synthesis of potentially dangerous gene products. "We screen the sequence, we identify critical sequences and do risk assessments, we screen the customers, check international denial lists and if all checks end up we send the sequence to the customer", Graf explained. "Customer screening is what governments require. That you don't do business with anyone on commercial denial lists. These lists come from intelligence agencies. [. . .] Once [customers] pop up on this list, we don't do any business with them". Likewise, people who do not have an academic or other relevant affiliation cannot order any products from companies associated with the IGSC.

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However, more work is needed, specially regarding the fact that 20% of the gene synthesis companies are not part of the IGSC. "It would be prudent to expand this to 100% via international (UN) consensus", commented Harvard Geneticist George Church. "Special efforts are needed for desktop instruments relative to centralized oligo synthesis. Both categories of device should be 'impossible' to operate until the sequences are checked with open-source and non-public algorithms".

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Having access to the technology and knowledge to create something dangerous is still a long way from actually creating it though. "Releasing a virus with the intent to cause harm is illegal", commented Todd Kuiken, Senior Research Scholar at the Genetic Engineering and Society Center, North Carolina State University, in the United States. "It's also not that simple. One would need rather sophisticated equipment to engineer, deploy and, importantly, protect themselves from such a virus (if they were even able to obtain it). All of which would require significant money". Moreover, as Kuiken pointed out, the DIY community is well aware of such risks. "It would be nearly impossible for someone to work on such a project in a community lab without someone noticing what they were doing and stopping it", he said. "From the earliest days of the DIYbio community, safety, security and responsibility have been a part of the community's ethics and discussions (see the codes of conduct developed in 2011 and subsequent codes developed at the community bio-summit)". To that end, the DIY movement has also welcomed help and advice from law enforcement agencies. "In the US, the FBI has had both an outreach program and working relationship with the community, dating back to about 2010/2011. Those relationships have reached beyond the US in the form of workshops that the FBI sponsored in which DIYbio groups from outside the US have attended", Kuiken added.

Nonetheless, the examples of biohackers creating DIY cures may still prove problematic, especially if they were emulated by others without caution and guidance. In addition, DIY genetics kits, such as those offered by The Odin Company, can be good and bad, depending on their use. The company, founded by Josiah Zayner, the biohacker who injected himself with a self-made herpes treatment, offers DIY kits for genetic engineering of animals and bacteria and provides Biohacker Classes and kits.

At the end of the day, though, the DIY biohacking community pursues the same goals of all scientists: to gain a better understanding of life and to use this knowledge to improve human lives. As Daniel Grushkin said in defense of [5]: "Rather than portraying community biology as a threat, it's time for the media—and the public—to see it as a public resource". Increasing awareness, monitoring by DNA synthesis companies, and the advice from law enforcement are, thus, helping to ensure that biohackers do not go astray.

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