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COMMENT

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Catalyzing pathways for translational research beyond COVID-19

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Emergency action in response to the COVID-19 pandemic led to the removal of financial and regulatory barriers to developing medical technologies. But, as Andrea Armani and Eric Diebold explain, a broader cultural shift in academia can expedite their translation from laboratory benches to real-world use.

The first lesson mentioned in any technology entrepreneurship class is the "push-pull" of technology development; simply, should an inventor wait for society to ask for an innovation or should they push their discovery out? This debate becomes increasingly complex when evaluating biotechnology that requires complex approvals and long development timelines, significantly increasing the financial cost of failure. However, during the Coronavirus Disease 2019 (COVID-19) pandemic, risk was no longer measured in dollars, but in lives, and this change motivated academia, companies, and governments to work together to accelerate solutions that normally would have taken years. But while the societal need served as the catalyst, one overarching question still remained: where should efforts begin? This question was quickly answered.

One common limiting factor in biotechnology development is familiarity with and acquiring government approval. With the establishment of the streamlined Food and Drug Administration's (FDA) Emergency Use Authorization (EUA) in the US[1], European Union Medical Device Regulation (EU MDR) 59, and regulatory changes around the world, this energy barrier was reduced. This approach had wide-ranging impact. It accelerated time-to-market authorization for personal protective equipment (PPE), diagnostics, therapeutics, and vaccines. It also opened the doors for non-biotech companies and academic researchers to contribute to the development of COVID-19-relevant technologies, as well as address wide-ranging supply chain shortages and manufacturing issues. This diversity of capabilities was first mobilized around a single, universal healthcare need: PPE.

As COVID-19 spread from China across the globe, we all watched in horror as the healthcare community faced shortages of a range of PPEs due to disruptions in manufacturing and in global supply chains. These images crystallized the first engineering challenge: developing new approaches for making and for re-using PPE, and for modifying existing manufacturing facilities. However, many research labs were closed, stranding engineers from critically needed research facilities. Thus, "working from home" took on an entirely new meaning as engineers began "researching from home" in garages and closets, and sourcing materials from local hardware stores. 3D printed designs for ventilators and face shields quickly emerged, and, in collaboration with researchers at the National Institutes of Health (NIH) who assisted in validation and review, EUA-authorized computer-aided designs appeared on the NIH 3D Print Exchange[2]. In larger cities like Los Angeles, industry experts designed injection molds to allow thousands of rims and plastic shields to be produced at scale. Notably, this entire effort was accomplished in under two months and was supported by a combination of government and private funding. It highlights a perfect example of academic, industry leaders, and government officials working together to

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address a crisis and sheds light on several different paths for expediting traditionally cumbersome collaborations (Fig. 1).

Three way tug of war

Usually academics (and society at large) place the responsibility for delays in making new medical technologies widely available on regulatory approval—or on the government. But during the past year, governments accelerated and streamlined the approval processes. This gave academia and industry a unique opportunity to take a step back and investigate what additional barriers limit technology translation in this time of need.

Academics are used to building "one" of something. This results in a fundamental mindset when considering costs, build-times, parts, and operation which permeates the entire design process. The manufacturing techniques are typically not evaluated, both in terms of materials needed as well as the complexity of the process, and the user interface and level of expertise needed to operate a system are not considered. Often, systems in academic labs are hand-built works of art and designed to operate in very controlled environments by PhD-level technical staff. This level of complexity increasing the bar when trying to displace an existing technology. With regards to the sub-field of biotechnology, many engineering-focused researchers are completely untrained in animal or human trials and thus are not always able to push a technique into clinical trials. Lastly, and perhaps most importantly, academic researchers are evaluated for tenure and rewarded for discoveries that demonstrate the "first" of something. This metric overlooks the importance of patents and the widespread adoption of technology.

In contrast, to consider a technology ready to translate, potential industry partners want to see findings replicated hundreds, if not thousands, of times in real-world settings by end users. This type of research is rarely funded or considered publishable in today's academic environment. Thus, these translational requirements often represent significant roadblocks that impact the attractiveness of a potentially transformative technology to industry partners. Yet, the past year has seen an unprecedented growth in development and translation for COVID-19 technologies. What changed to reduce the gap between academia and industry and what institutional changes can continue this trajectory into the future?

Changing our values

Looking back on the past year, one word summarizes the technology community: teamwork. This philosophy accelerated a wide-range of innovations, from disinfection methods to vaccines. Powered by unprecedented financial increases in research support, by high participation rates in patient trials, and by emergency regulatory authorizations, unconventional partnerships arose to bridge gaps in running large pilot trials and to develop manufacturing strategies. Additionally, this combination of funding and reduced timeline to market authorization de-risked many early-stage technologies, making them more attractive to industry members despite lingering manufacturing concerns.

One of the initial technology success stories was ultra-violet (UV)-C disinfection for medical settings. Originally proposed in the early 1900s, UV-C-based methods are commonly found in environmental disinfection systems, including water and air purification. In contrast, use in medical settings has been limited for a range of reasons, including user interface and relative cost to comparable methods. Additionally, the medical community's confidence with chemical methods further increased the barrier to adding a new and unknown technique. However, shortages in disinfection chemicals forced healthcare workers to explore alternatives. In the first few months of the pandemic, several systems were developed and validated by engineers from academia and industry working in collaboration with medical centers. The designs were wide-ranging from low-cost portable containers[3] capable of disinfecting a variety of items to largescale cage systems that were optimized for N95 masks[4]. In most cases, industry partnerships accelerated manufacturing and distribution of the systems in their local area[3]. However, to reach the global community, collaborations with international technical societies were initiated. Notably, the majority of the systems were not patented, but instead the schematics were posted on arXiv or society webpages, creating the equivalent of open-source for hardware.

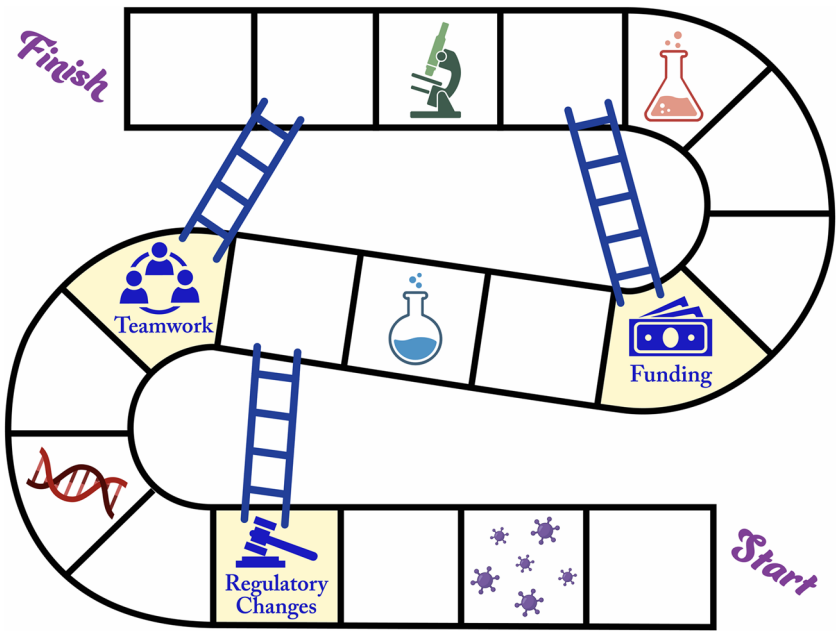

Fig. 1 Roadmap of technology translation. Translating a technology involves numerous steps. During the past year, several new paths were opened, accelerating this process. Created using icons from BioRender.com.

This shock to the system also inspired many in academia to reset priorities and redirect their research focus. Instead of pursuing high-impact factor articles and medals, some research teams began to place an increased emphasis on translation and societal impact. This dramatic shift was only possible because of the sudden influx of government research support and encouragement in this direction. One highly impactful example of this academic-government collaboration (enabled by the rapid advances in COVID-19 diagnostics) was the creation of the Johns Hopkins Coronavirus Resource Center, which provided real-time quantitative data, enabling the public, policy makers, and scientists alike to track COVID-19 spread globally[5]. Additionally, many academic research groups "loaned out" their team members and equipment to aid in diagnostic labs during regional surges and to serve as interns to accelerate biotechnology research. As a result, the students and post-doctoral scholars that have been trained during this time have received a very cross-cutting, real-world-centric educational experience that will serve the biotechnology innovation community by creating a grounded, and uniquely qualified, workforce for the future.

In addition to catalyzing academic-industry partnerships, EUA's also fast-tracked collaborative partnerships between companies, accelerating the development of diagnostics and vaccines. One of the first real-time polymerase chain reaction (RT-PCR) tests for COVID-19 was the result of two collaborations—BD (Becton, Dickinson and Company) and BioGX Inc. in the US, and BD and CerTest Biotec outside the US. When COVID-19 emerged, the two partnerships were able to move their assays through the validation and regulatory processes much faster together than they would have independently to better meet worldwide demand. There is perhaps no more notable and compelling example of teamwork than the partnership between Pfizer and BioNTech, in which novel mRNA vaccine technology came to market in record time due to the collaboration and partnership of two commercial entities, alongside the government's willingness to expedite approvals under the FDA's EUA. The complex and challenging development and rollout of this life-saving vaccine have been nothing short of a multi-national miracle and proves what can be accomplished through the ultimate demonstration of teamwork at the grandest of scale.

To continue this impact in the future, industry and academia need to work together, not only on translating technologies but also on improving the relevancy of academic training. A clear demand has emerged for highly skilled technicians and engineers in specialty fields. Not surprisingly, one area that came to the forefront during the past year was manufacturing engineers and technicians. These positions require an extremely diverse skill set, often inclusive of mechanical, electrical, and biomedical engineering as well as computer science and robotics. Despite the creation of the federally-funded Manufacturing Institutes headquartered at academic institutions, relevant training is not offered at most US-based universities and colleges, leaving employers to rely on students to obtain the requisite skills through extracurricular pursuits. To overcome this barrier requires academia to develop entirely new curricula to meet the needs of industry partners and to motivate students to recognize the value in these career paths.

Conclusions

The past year witnessed an unprecedented battle between the scientific community and a single virus. Through the cumulative achievements of research, development, manufacturing, and healthcare communities, society is slowly emerging on the other side of this global pandemic. But there are many more healthcare challenges to overcome. Unfortunately, the teamwork that has been the hallmark of the past year and that is responsible for the rapid advancement of many technologies is unlikely to be sustained when working on other disease systems where emergency regulatory authorization is not an option. However, while improving regulatory science is necessary, it is only one component of this complex landscape that also relies heavily on research funding and a skilled workforce.

Through this experience, we discovered our collective potential, and it is nearly limitless when we work together towards a common goal. Thus, it is imperative that we continue this momentum as we re-focus our energy on challenges in healthcare, sustainability, and education. Continued success will require creating an environment that fosters innovation and teamwork, and it will rely on reducing regulatory hurdles, increasing support for applied research and manufacturing, and modernizing training content—all for the benefit of the future of our society.

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References

1. Office of the Commissioner. *Emergency Use Authorization* (FDA, 2021).
2. Armani, A. M., Hurt, D. E., Hwang, D., McCarthy, M. C. & Scholtz, A. Low-tech solutions for the COVID-19 supply chain crisis. *Nat. Rev. Mater.* **5**, 403–406 (2020).
3. She, R. et al. Lightweight UV-C disinfection system. *Biomed. Opt. Express* **11**, 4326–4332 (2020).
4. Purschke, M. et al. Construction and validation of UV-C decontamination cabinets for filtering facepiece respirators. *Appl. Opt.* **AO 59**, 7585–7595 (2020).
5. Dong, E., Du, H. & Gardner, L. An interactive web-based dashboard to track COVID-19 in real time. *Lancet Infectious Dis.* **20**, 533–534 (2020).

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Competing interests

The authors declare the following competing interests: Eric D. Diebold is an employee of Becton, Dickinson and Company. Andrea M. Armani declares no competing interests.

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