ToughTech

A publication by The Engine, built by MIT

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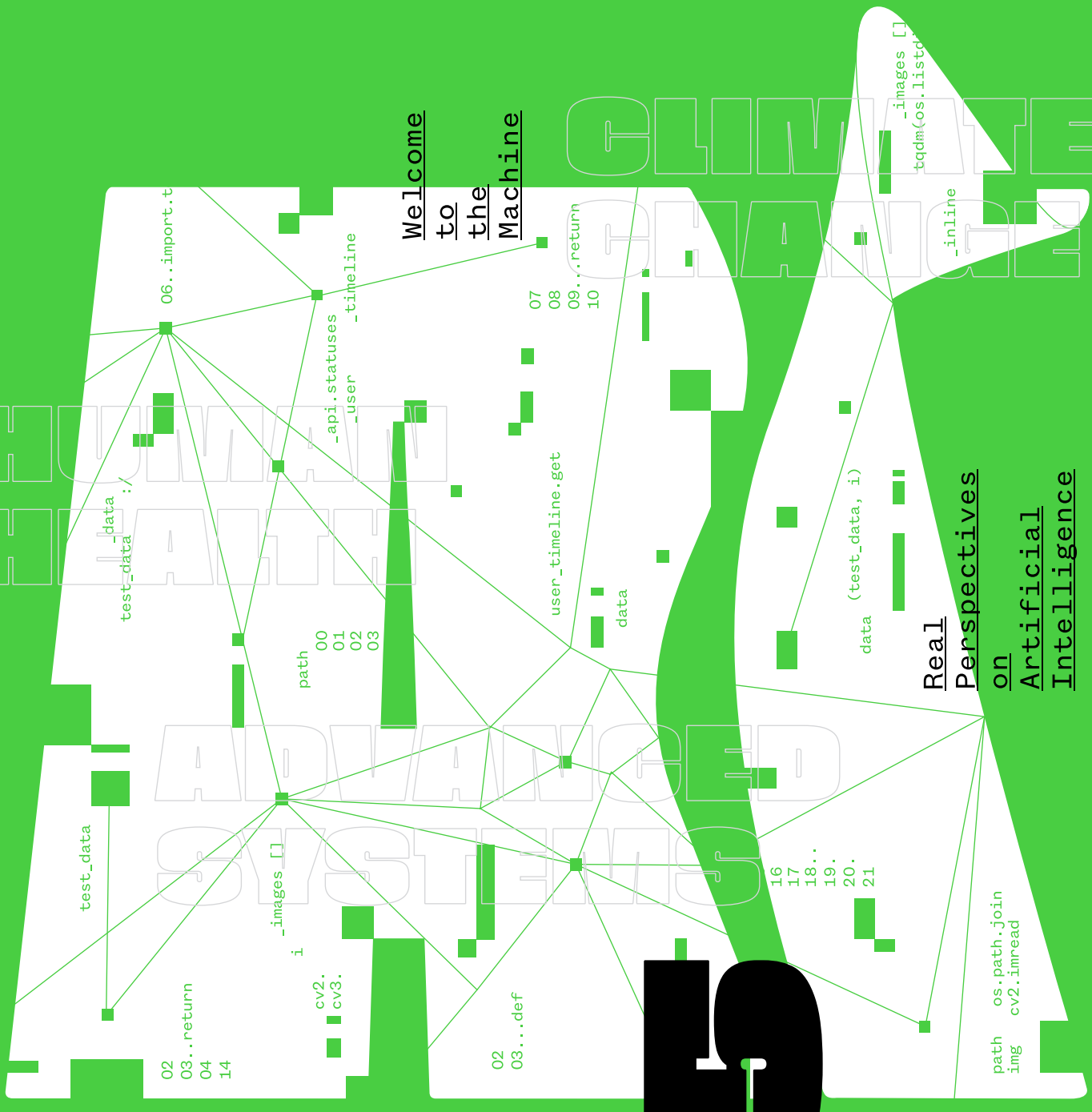

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THE ENGINE
Built by MIT

A home for Tough Tech founders.

The Engine, built by MIT, is a venture firm that invests in early-stage companies solving the world's biggest problems through the convergence of breakthrough science, engineering, and leadership. Our mission is to accelerate the path to market for Tough Tech companies by providing access to a unique combination of investment, infrastructure, and a vibrant ecosystem.

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THE AI ISSUE

Artificial intelligence is a general purpose technology with incredible possibilities. Its story winds through academic laboratories, halls of philosophy and mathematics, and our planet's most significant industries. It touches our homes and even our bodies. It is everywhere and, as some predict, will become everything.

There are vital and vigorous debates as to the societal, cultural, and moral implications of artificial intelligence. This publication largely sidesteps those conversations in favor of providing an overview of how AI has, and will, unbridle industries and technologies, namely those we call Tough Tech. Think of it as a primer — providing context for the profusion of AI approaches, technologies, and businesses.

How will AI help us develop new approaches to combat challenges like climate change, disease, and the limits of computing itself? What shape are these new Tough Technologies taking? This publication attempts to build a common understanding of AI in an effort to answer these questions.

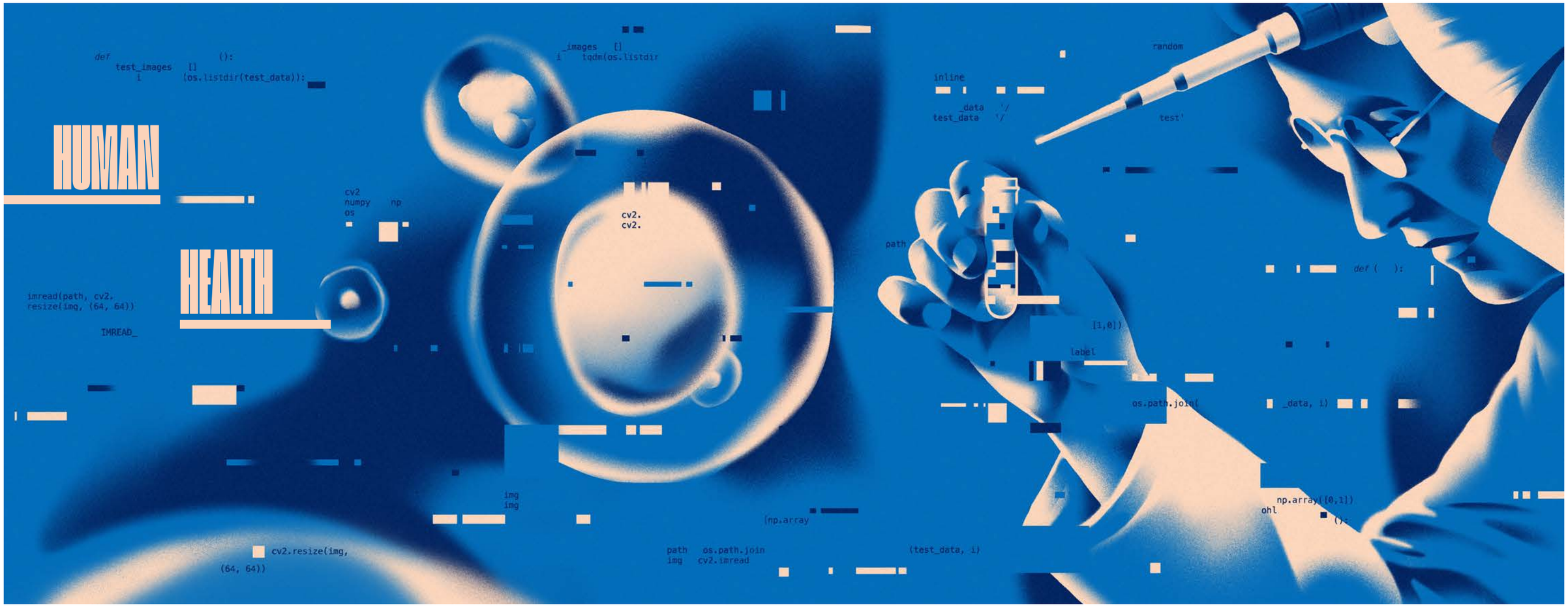
"We can only see a short distance ahead, but we can see plenty there that needs to be done."

Alan Turing

WELCOME TO THE MACHINE

AI is redefining how we fight climate change and combat disease. It is even revolutionizing the systems responsible for its own evolution.

by Michael Blanding
Illustrations by Harol Bustos



Depending on whom you talk to, the number of possible chemicals in the world are anywhere from 10^{60} to 10^{80} — somewhere, in other words, between the number of atoms in our solar system and the number of atoms in the visible universe. Any one of those chemicals could hold the key to development of a new drug or other therapy. While human researchers often have a good intuition of where to explore, the sheer vastness of the space leaves ample room for AI to assist in discovering brand-new possibilities that humans might not have even considered.

"In drug discovery, you're going to have all of these ideas of what could be a good candidate molecule," says Connor Coley, an assistant professor of chemical engineering at MIT. "You know what could have good bioactivity, good potency, good solubility, and other properties, — but in order to test it, you actually have to make it." Creating drugs can be a complicated process, requiring multiple chemical reactions in a specific sequence and conditions, done at scale in order to synthesize the desired amount of drug to test.

Coley previously worked in the laboratory of Klavs Jensen, an MIT professor applying those principles to the synthesis and discovery of small molecules, which form the basis of many medicines. Using supervised learning techniques, he and his colleagues have used AI to simulate the testing of candidate molecules, varying catalysts, temperature, and concentration and predicting likely outcomes. "All of those variables will have some effect on the yield, efficiency, and cost of running that reaction," says Coley. "These adaptive algorithms help you design experiments and tell you what are the most useful experiments to run."

↳ RESEARCHERS ARE USING AI TO SPEED UP DEVELOPMENT OF NEW DRUGS AND OTHER THERAPIES. DEPENDING ON WHOM YOU TALK TO, THE NUMBER OF POSSIBLE CHEMICALS IN THE WORLD ARE ANYWHERE FROM 10^{60} TO 10^{80} – SOMEWHERE, IN OTHER WORDS, BETWEEN THE NUMBER OF ATOMS IN OUR SOLAR SYSTEM AND THE NUMBER OF ATOMS IN THE VISIBLE UNIVERSE.

More recently, Coley and his colleagues have been using supervised machine learning on a huge corpus of chemical reactions collated by Elsevier and other companies to help identify new molecules to test. "We're taking information chemists have been publishing for the last couple hundred years, and then trying to apply that to new molecules," Coley says. "Then we put out a full synthetic recipe about how you might be able to make it—everything you should buy, how you should combine them, and what steps you should take to produce the molecule of interest." More recently, Coley and his colleagues, including Jensen, have worked on creating a robotic platform[3] similar to Aspuru-Guziks' self-driving laboratory to at least partially automate that process. "The idea is to make the research and development process a little bit easier and a little bit faster."

Coley is a member of MIT's Machine Learning for Pharmaceutical Discovery and Synthesis Consortium, a group that includes both MIT researchers and representatives from 14 pharmaceutical and biotech companies to help better train algorithms to discover and create new drugs. The companies provide financial support as well as feedback from their own processes to the labs, which produce models and algorithms for use of members. "We benefit tremendously from understanding what are the real pain points in their workflows, and how well the existing solutions work to alleviate those pain points," Coley says. In return, such techniques could help companies to quantitatively determine which candidates for drug discovery they should pursue for testing.

Another consortium member, MIT computer science professor Regina Barzilay, recently led the use of deep learning techniques to discover a new antibiotic. Historically, antibiotics have been discovered by screening vast numbers of soil-dwelling microbes, or creating synthetic varieties based on those discoveries that she, James Collins (a Professor of Medical Engineering and Science at MIT), and colleagues wrote about in a paper published in *Cell* in February 2020[4]. As the number of new molecules have shrunk, however,

3. http://news.mit.edu/2019/automate-molecule-production-ai-0808
4. https://www.cell.com/cell/pdf/S0092-8674(20)30102-1.pdf

—Real Perspectives on Artificial Intelligence—

Rick Calle
Artificial Intelligence
BD @ M12

Dayna Grayson
Founder @ Construct Capital

Randy “Laz” Gordon, Colonel USAF
Director @ USAF/MIT Artificial
Intelligence Technology Accelerator

Rohit Prasad
VP & Head Scientist @ Alexa AI

Dan Huttenlocher
Dean @ MIT Schwarzman
College of Computing

Daniela Rus
Professor Electrical Engineering
and Comp Sci & Director @ MIT CSAIL,
Deputy Dean @ MIT Schwarzman
College of Computing

For extended interviews,
visit medium.com/@the_engine

Texts edited for length and clarity
Illustrations by Harol Bustos

Interviewed 3.30.2020

DAN HUTTENLOCHER

Dan is the inaugural dean of the MIT Schwarzman College of Computing. Previously he helped found Cornell Tech, the digital technology oriented graduate school created by Cornell University in New York City, and served as its first Dean and Vice Provost.

■ *No matter how responsibly developed AI may be, its generality seems at once its greatest asset and its greatest danger. How do you reconcile this duality?*

■ I think it's a great question. Much of this — and I don't know if it's fear of AI, exactly — but much of the sense of the potential dangers of AI comes from a misunderstanding of what the technology really is. There's often a tendency to anthropomorphize technology and with AI this tendency is much more extreme. In the end these are still just algorithms. When we're using machine learning, for example, they are algorithms that we can teach instead of algorithms that we have to code. But they're still algorithms. They're not going to become evil. There's no rational basis for that worry at the present time (I'm not saying it's impossible for that to be true in some future with technologies one cannot foresee today, but for the path we are on it is science fiction). If these algorithms are used for something bad, it's because people decided to use them for something bad. They don't decide to do things that are bad on their own.

■ *I've heard similar sentiments expressed throughout the AI community. On one hand this sentience like Data from Star Trek or the Terminator robot is far fetched, but it's also so ingrained in popular culture, that it's hard to think about AI any other way.*

■ It's easy to anthropomorphize AI when you have an Alexa or Google Home or something similar in your house answering your questions. And just imagine when these tools become robots that you're conversing with — which won't be long, I'm sure. It's natural that people will then assume that these machines have the full range of human intelligence. People already anthropomorphize their Roombas. How these intelligences will evolve, especially considering how machine learning has grown lately, poses some interesting questions. Many of these platforms are now learning from us rather than being programmed — they learn what we do, not what we aspire to do, not what we say we're going to do. They are not necessarily learning our best attributes, they are learning our actual selves. And that can be embarrassing.

■ *And these attributes can be interpreted as biases.*

■ Yes. Biases we may not even know we have. Or biases we do know we have some of which we legislate against. So when you start observing behaviors and decision making behaviors by humans to train machine learning, there's all kinds of bias there, which may be undesirable. Once we recognize that these platforms are surfacing biases then we can get more systematic in combating those biases. It's what good actors are doing now. And what legislation will eventually require. I think we're in a time period now where people are rightly agitated — and that's good because it's highlighting things that need attention in the world, not only attention in AI. I think AI will continue to evolve in a positive way — we'll end up in a much better place than today.

■ *I like the optimism! A bit of a pivot here — will AI, like calculus or geometry, become a prerequisite for every engineering program?*

■ Yes, I think so. And I would broaden this beyond AI to encompass "computing" in general. Even now it is something that every student needs to learn. As AI gets to be a more and more important part of computing, it too will become required. MIT already has a large percentage of undergraduates studying machine learning. In many senses, computing is already a de facto requirement.

■ *So much has changed since your time as a student in MIT's AI Lab. What's surprised you the most since you left?*

■ The big surprise is how quickly AI became practical. As a grad student in the 1980s, we joked around that AI was the perfect research problem, because it would always look like it was almost ready. Now here we are, a few decades later, and AI is used everywhere.

■ *The final question: in 20 or 30 years, do you see any industries or sectors being AI holdouts? Those in which AI will be difficult to implement for technological or cultural reasons?*

■ For technological reasons? I can't think of anything. Maybe if there's some big AI backlash, maybe we'll see some sort of Neo Luddites who are specifically anti-AI, that is certainly not impossible.+

HUMAN HEALTH

Biobot Analytics
Cambridge Crops
Cellino
E25Bio
Kytopen
Lucy Therapeutics
Seaspire Skincare
Suono Bio
Vaxess Technologies

CLIMATE CHANGE

Boston Metal
Cambridge Electronics
Commonwealth Fusion Systems
Form Energy
Lilac Solutions
Syzygy Plasmonics
Via Separations

ADVANCED SYSTEMS

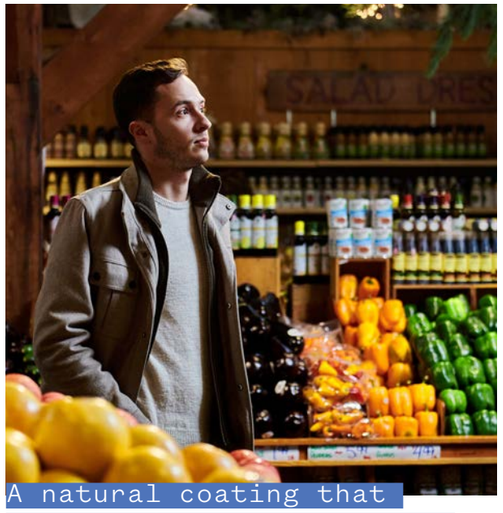
Analytical Space
C2Sense
HyperLight
isee
Radix Labs
RISE Robotics
Sync Computing
Zapata Computing

The Portfolio Companies

The Engine invests in founders solving the world's biggest problems through the convergence of breakthrough science, engineering, and leadership.

We've seen our investments coalesce into three areas of impact: those companies whose core technology will help solve climate change; those that will create new human health solutions; and those that will usher in a new era of advanced systems.

HUMAN HEALTH



A natural coating that reduces food spoilage and packaging waste.

Cambridge Crops

Founders
Adam Behrens, Sezin Yigit, Benedetto Marelli, Livio Valenti, Fiorenzo Omenetto

Background
MIT Laboratory for Advanced Biopolymers, Tufts University SilkLab

Industry
Food & Agriculture, Advanced Materials

Cambridge Crops is addressing the problem of food spoilage and waste by pioneering a natural, ultra-thin water-based coating that preserves the freshness of food longer. It's tasteless and invisible and can be applied to everything from fresh and cut produce to proteins like meat and fish. The coating dramatically extends shelf life by slowing the exchange of gases that cause decay, making food accessible to more people for longer times. In addition, the coating has the potential to support enhanced nutrients for food and also help reduce packaging.

Significance
One third of the food produced in the world is wasted. Cambridge Crops' technology helps to reduce food spoilage across the supply chain, decreases logistics costs, and makes healthy food more accessible.

Cellino

Founders
Nabiha Saklayen, Matthias Wagner, Marinna Madrid

Background
Harvard Physics Department, Harvard School of Engineering and Applied Sciences (SEAS), Harvard Medical School

Industry
Biotech & Life Sciences, Advanced Manufacturing, AI & ML

Cellino has built the first platform that enables precise control over iPS cell fate in their natural environment. The Cellino Tissue Engineering Platform manufactures high-quality, impurity-free tissues for new regenerative medicines. Cellino will use its platform to manufacture tissues at scale, delivering the highest quality human tissues made to date. Such tissues are poised to lead to significant gains in therapeutic benefit to the patient.

Significance
Cellino's approach for high-throughput, computer-guided engineering human cells will create new tissues with significant gains in therapeutic benefit to the patient and further transform the biotech industry.

A tissue foundry for regenerative medicine.

Rapid, accurate diagnosis of infectious disease at the point of care.

E25Bio

Founders
Irene Bosch, Bobby Brooke Herrera, Lee Gehrke

Background
MIT Institute for Medical Engineering & Science, MIT Tata Center

Industry
Biotech & Life Sciences

E25Bio is pioneering an at-home rapid fever panel for mosquito-borne diseases. With its first-in-class antibodies identified with a novel screening method, E25Bio's diagnostic test is the first of its kind to distinguish between dengue (as well as all four subtypes of the disease), chikungunya, and Zika.

Significance
E25Bio is reducing a specialized central medical testing facility to a single over-the-counter test. Initially, the company's rapid fever panel will empower patients, healthcare workers, and public health officials in Latin America. But the company's ability to quickly discover and produce effective antibody pairs means that it has the potential to help patients across the globe.

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