The Worldview 100: Who are the Most Influential People in Biotech Today?

The Power of Communication | DNA as Anti-Aging Software | Beating Blood Cancer

+ The 7th Annual Worldview Scorecard
The definition of "conundrum" is "a confusing and difficult problem or question."—a definition that clearly applies to the growing number of cancer patients who are prescribed state-of-the-art cancer medicines and yet, delay taking them or don’t take them at all.

According to the latest projections, nearly half of Americans diagnosed with a chronic disease take their medicine as directed only 50 percent to 60 percent of the time. The consequence of this poor medication adherence is more doctor visits, trips to the emergency room, and hospitalizations, all of which is estimated to cost the health care system between $100 billion and $300 billion annually.

However, for Americans fighting a deadly cancer, the consequences can also be life-threatening and thus, the conundrum: Why are cancer patients skipping doses or taking less than the prescribed amount of their cancer medicines? The answer is simple: In the name of cost-containment, insurance companies increasingly restrict patients’ access to breakthrough cancer medicines through high copays and practices that require patients to fail on medication after medication until they first fail on several inferior medicines and treatments before it will pay for the drug that the doctor originally prescribed. Equally onerous is placing new cancer medicines into the highest pharmacy ("specialty") tier and forcing patients to pay a large percentage of the drug’s price. According to a recent Leukemia & Lymphoma Society report, even the new state exchange plans implemented under the Patient Protection and Affordable Care Act for previously uninsured patients use this cost containment strategy. This means patients can pay up to 50 percent of the costs of new cancer therapies, which leads to poor adherence.

Then, there is the practice of shifting as much as 25 percent of the cost of oral anti-cancer medicines to patients in high co-pays—even though these drugs are less invasive than intravenous infusions, they carry fewer side effects, and patients don’t have to travel to the doctor’s office every week, resulting in time away from work or family. Yet, because the co-pays can be hundreds or thousands of dollars per month, studies find almost 10 percent of insured patients choose not to fill their initial prescriptions for oral anti-cancer medications.

To save lives, the patient community, cancer advocacy groups, and public health organizations are pressing Congress and state legislators to cap copays on specialty medicines and ensure equality of access and insurance coverage for all anti-cancer regimens. To date, 39 states and Washington, D.C. have enacted oral chemotherapy access laws, while 15 states and the District of Columbia have either introduced or passed bills to limit what patients pay for specialty medicines.

The Alliance for the Adoption of Innovations in Medicine supports these policies because adhering to cancer medicines is a necessity. It is clear that the transformative change of precision medicine is well underway—rightfully confronted with rising copays, restricted coverage and all too often, insurance practices that deny access completely. This is the bitter reality of today’s access fights—with patients and their doctors denied medications every day by a complex coverage and reimbursement insurance system that has either introduced or passed bills to limit what patients pay for specialty medicines.

In response, a patient revolution has ignited and touched down in 39 states and Washington, D.C. to address the problem of inequitable coverage by requiring health plans to equalize the patients’ out-of-pocket costs between oral and intravenous therapies. Further state-by-state reform efforts will surely follow.

As a nonprofit organization working to improve cancer care, Vital Options International (VOI) believes patients should not be forced to battle the system and their cancer at the same time. This is why VOI supports energetic and innovative movements underway to update the drug approval process using 21st century computing capabilities, genomic analysis and a new understanding of cancer on a molecular level.

We also hope legislators and regulators will work with doctors, patients, caregivers and payors to provide faster and easier access to the latest medications—and do so in a way that prioritizes patient safety and supports the integrity of new drug evaluations.

To almost countless patients, there is only one obvious move left: Towards a regulatory future that embraces access and accepts nothing less than the right patient, the right medicine and right now.
4 LET’S GIVE ‘EM SOMETHING TO TALK ABOUT…  
BY JEREMY ABBATE, MIKE MAY & YALI FRIEDMAN

5 yourVIEWS:  
Letters, Opinions, Critiques

8 SPECIAL REPORT: THE WORLDVIEW 100  
The visionaries who continue to reshape biotechnology  
—and the world

8 THE WORLDVIEW 100

86 PRODUCTS OF THEIR ENVIRONMENT
How R&D location impacts which drugs are produced.  
BY YALI FRIEDMAN

88 LAWS OF ATTRACTION
How a nation’s policies attract and discourage biopharma investment  
BY MEIR PEREZ PUGATCH, DAVID TORSTENSSON, RACHEL CHU, AMIR DAYAN & NOA WEINSTEIN

22 FROM EUREKA TO USEFUL
Developing an idea into a productive tool demands experience, foresight and a persistent champion  
BY MIKE MAY

26 ROOM TO GROW
LabCentral gives start-ups the space and resources to thrive  
BY JOHANNES FRIEDEHAUF

28 BIOTECHNOLOGY’S CRUCIAL QUESTION
In this industry, what matters the most: technology or people?  
BY STEPHEN M. SAMMUT

44 AN EVENING WITH TOP MEDICAL INNOVATORS
Today’s visionaries battle cancer with cutting-edge science and the stubbornness to make it work  
BY MIKE MAY

54 CONTACT US!
We invite letters & opinions from all of our global readers.
WRITE US AT: saworldview @sciam.com

64 36 THE 7TH ANNUAL GLOBAL BIOTECHNOLOGY SURVEY

66 PRODUCTS OF THEIR ENVIRONMENT
How R&D location impacts which drugs are produced.  
BY YALI FRIEDMAN

68 LAWS OF ATTRACTION
How a nation’s policies attract and discourage biopharma investment  
BY MEIR PEREZ PUGATCH, DAVID TORSTENSSON, RACHEL CHU, AMIR DAYAN & NOA WEINSTEIN

72 AN EVENING WITH TOP MEDICAL INNOVATORS
Today’s visionaries battle cancer with cutting-edge science and the stubbornness to make it work  
BY MIKE MAY

76 Dispatches from: China, Germany, India, Japan, Norway, Poland, Romania, Russia, Scotland, United States

84 AGING 2.0
Stem cells and digitized DNA may hold the key to high-performance longevity  
BY ROBERT HARIRI

86 SPECIAL REPORT: THE WORLDVIEW 100

88 PRODUCTS OF THEIR ENVIRONMENT
How R&D location impacts which drugs are produced.  
BY YALI FRIEDMAN

90 LAWS OF ATTRACTION
How a nation’s policies attract and discourage biopharma investment  
BY MEIR PEREZ PUGATCH, DAVID TORSTENSSON, RACHEL CHU, AMIR DAYAN & NOA WEINSTEIN

108 A HEALTHY DIALOGUE
How the healthcare media impacts policymakers and the public  
BY ELIE DOLGIN

110 COMMUNICATION BREAKDOWN
Looking at the GMO controversy through the lens of communications science  
BY ANDREW D. ROBERTS & ANDREW D. POWELL

112 THE TRICKY SCIENCE OF COMMUNICATION

122 AN EVENING WITH TOP MEDICAL INNOVATORS
Today’s visionaries battle cancer with cutting-edge science and the stubbornness to make it work  
BY MIKE MAY

132 Dispatches from: China, Germany, India, Japan, Norway, Poland, Romania, Russia, Scotland, United States

144 AGING 2.0
Stem cells and digitized DNA may hold the key to high-performance longevity  
BY ROBERT HARIRI

146 SPECIAL REPORT: THE WORLDVIEW 100

148 PRODUCTS OF THEIR ENVIRONMENT
How R&D location impacts which drugs are produced.  
BY YALI FRIEDMAN

150 LAWS OF ATTRACTION
How a nation’s policies attract and discourage biopharma investment  
BY MEIR PEREZ PUGATCH, DAVID TORSTENSSON, RACHEL CHU, AMIR DAYAN & NOA WEINSTEIN

162 A HEALTHY DIALOGUE
How the healthcare media impacts policymakers and the public  
BY ELIE DOLGIN

164 COMMUNICATION BREAKDOWN
Looking at the GMO controversy through the lens of communications science  
BY ANDREW D. ROBERTS & ANDREW D. POWELL

166 THE TRICKY SCIENCE OF COMMUNICATION

176 WORLDBUSINESS EVENTS

178 WORLDBUSINESS EVENTS

180 CONTACT US!
We invite letters & opinions from all of our global readers.
WRITE US AT: saworldview @sciam.com

182 worldVIEW

184 worldVIEW

186 worldVIEW

188 worldVIEW

190 worldVIEW

192 worldVIEW

194 worldVIEW

196 worldVIEW

198 worldVIEW

200 worldVIEW

202 worldVIEW

204 worldVIEW

206 worldVIEW

208 worldVIEW

210 worldVIEW

212 worldVIEW

214 worldVIEW

216 worldVIEW

218 worldVIEW

220 worldVIEW

222 worldVIEW

224 worldVIEW

226 worldVIEW

228 worldVIEW

230 worldVIEW

232 worldVIEW

234 worldVIEW

236 worldVIEW

238 worldVIEW

240 worldVIEW

242 worldVIEW

244 worldVIEW

246 worldVIEW

248 worldVIEW

250 worldVIEW

252 worldVIEW

254 worldVIEW

256 worldVIEW

258 worldVIEW

260 worldVIEW

262 worldVIEW

264 worldVIEW

266 worldVIEW

268 worldVIEW

270 worldVIEW

272 worldVIEW

274 worldVIEW

276 worldVIEW

278 worldVIEW

280 worldVIEW

282 worldVIEW

284 worldVIEW

286 worldVIEW

288 worldVIEW

290 worldVIEW

292 worldVIEW

294 worldVIEW

296 worldVIEW

298 worldVIEW

300 worldVIEW

302 worldVIEW

304 worldVIEW

306 worldVIEW

308 worldVIEW

310 worldVIEW

312 worldVIEW

314 worldVIEW

316 worldVIEW

318 worldVIEW

320 worldVIEW

322 worldVIEW

324 worldVIEW

326 CONTENTS
LET'S GIVE 'EM SOMETHING TO TALK ABOUT...

We want to encourage readers to explore biotechnology from a broad and global perspective.

...patients are unique genetinically and environmentally, and hence should not be averaged in large populations.

worldVIEW

In our article “Transforming Medicine: A Manifesto” (Scientific American Worldview, 2014), we challenged the foundation of “evidence-based medicine.” We noted that methods used to generate this evidence, the basis for...
Our healthcare system is strapped with the burgeoning costs of chronic care and will ultimately seek more cost-effective approaches. As of 2006, patients with chronic diseases accounted for 84% of all healthcare spending. By leveraging our ability to rapidly sequence laboratories in the United States and United Kingdom to discover solutions to extend people’s healthy life span.

The Disease Intervention Accelerator (DIA) is a new incubator-like group based in New Jersey that seeks to identify the root causes of disease and enable the development of interventions that stop the progression to disease. Our first disease area of focus for the DIA is type 1 diabetes (T1D).

Scientists will work to develop new diagnostic, being the first company to develop baby products that allowed for “no more tears,” through the Band-Aid and disposable contact lenses, medical devices and blood typing, to developing the first treatment for tuberculosis in 40 years. It is our responsibility as a leading healthcare company to continue to drive innovation and make a difference for people and society.

As an industry, we have accomplished great things and have laid the foundation for a bright future. The launch of ambitious, forward-thinking initiatives will further propel us into a bold new era of research and development—an era marked by the promise of new firsts, including a day when the term “patient” is a historical artifact.

Even now, with more than 10,000 people dead and 24,000 confirmed cases of Ebola in eight countries, it is still not clear who will pay for, or when, a vaccine becomes available. Millions of doses will be needed, and not everyone will be there, and at the same time paying we never have to use them.

Seth Berkley CEO Gavi, the Vaccine Alliance Geneva, Switzerland

IPSCs and Personalized Medicine

President Obama’s Precision Medicine Initiative recently pledged US$15 million to fund research to use personalized genetic information as the starting place for understanding individual response to disease and treatment. While the initiative is necessary, it fails to address the questions that DNA and genetics alone cannot answer, questions that must be posed at the cellular level, where the answers may dramatically improve patient healthcare. Induced pluripotent stem cells (iPSCs), with the potential to be manufactured from virtually any patient’s blood cells, set the stage for research to make enormous gains in understanding how to approach medical treatment.

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Hematology Trial Nuances

Louis J. DeGennaro’s “Embracing the Process” (Scientific American Worldview, 2014) draws much needed attention to the lack of targeted treatment options available for acute myeloid leukemia (AML). I applaud the steps the Leukemia & Lymphoma Society is taking to address these unmet medical needs. While significant progress has been made, and the United States needs to lead this race to the finish line.

Bob Palay CEO and Chairman Cellular Dynamics International (CDI) Madison, Wisconsin

Contact us at: saworldview@sciam.com
The WorldView 100

The Visionaries Who Continue to Reshape Biotechnology—and the World

At just 40 years old, biotechnology is a relatively new industry. Its starting point, arguably, was the 1975 Asilomar Conference on Recombinant DNA, at which the potential benefits and hazards of DNA manipulation and the ways it should be regulated were debated and essentially decided upon. Most of the seminal figures in the development of biotechnology are alive today. Indeed, many of them are still working in the field that they love.

Here, we name 100 of the industry’s leading lights in a list we’ve dubbed “The Worldview 100.” The honorees include researchers who provided fundamental insights into biological processes, as well as their colleagues who developed those insights to create the biology-based goods and services that are the essence of biotechnology. We also recognize the business experts who had the foresight to provide financial backing in this high-risk, nascent technology sector, along with the entrepreneurs who constructed and implemented the business principles that made those investments pay off. Dotted throughout are several visionary legislators and administrators who understood the need to create fertile conditions enabling biotechnology to flourish, and a number of key media figures who have helped to convey its potential and successes to the community at large. The realm of biotechnology extends so far that some people on our list might not even consider themselves part of this industry. Nonetheless, these scientists and business builders are as complementary to the emergence of the field as two parents are to a child.

Advances in biotechnology are the results of the efforts of many tens of thousands of people. The Worldview 100 could easily have been developed as The Worldview 500, The Worldview 1,000, or any multiple thereof. In identifying just 100 individuals, our intention is to illustrate the range and quality of its leaders, rather than to offer a definitive register of its “most important” contributors. Nevertheless, the list stands scrutiny as a collection of extraordinarily talented and effective people. To learn more about them, we provided each with an opportunity to respond to a few questions—some serious and others less so—and we share some of their answers.

What traits do these leaders have in common? Creativity and enterprise are givens. Resilience and self-sacrifice are also critical, as the complexity of the science and its regulation demands that they constantly strive to maintain momentum, however far away their goal appears. And since risk-taking is practically the norm in biotech, these figures have to possess the confidence to outdare the crowd, to blaze a trail and to maintain their nerve, sometimes against overwhelming odds. Emotional intelligence is another prerequisite for The Worldview 100, who invariably have the ability to get along with others and the forthrightness to be constructive—critical when necessary.

One suspects that many of biotech’s key players would have stood out in whichever career they chose. So what enticed them into this field? Perhaps its newness, offering the thrill of putting a personal stamp on a fledgling industry, was part of the attraction. But surely the biggest draw was the scope and potential impact of the work: re-envisioning health and wellness, transforming agriculture, retooling traditional industries and providing solutions to the global energy crisis in a climate-friendly manner. What greater challenges does our world face?

We present The Worldview 100, who are facing them head-on.

—The Scientific American Worldview team with key contributions from Alexandra Hariri and Richard Gallagher.
George Church started his career with sequencing, especially through the development of advanced devices, and he continues to help scientists collect and analyze data about the most basic life traits. As the director of PersonalGenomes.org, he provides open access to data that explore the foundation of human traits around the world. His work on next-generation sequencing and cellular and tissue engineering spawned a dozen companies based on medical genomics or synthetic biology. Kirkus Reviews called his book _Regenerate_ a "valuable glimpse of science at the edge."

"I think my greatest contribution to biotechnology arose from the charge I was given to lead the international Human Genome Project," Collins told _Scientific American Worldview_. "Through the dedicated work of 2,400 scientists in six countries, we successfully sequenced and made immediately available the 3 billion base pairs in the human genetic blueprint—ahead of schedule and under budget!" To make biotechnology even more effective, he said, "It is especially important to support the creative minds who are pursuing high-risk projects that, if successful, may yield high rewards for expanding biological knowledge or fighting human disease."

"A valuable glimpse of science at the edge."

"The goal is not just butterfly collecting or mammal collecting to simply describe mammals. All of that comparative work across mammals is about informing the human genome for medicine. Until we actually understand all the working parts within our genome, we won't really be able to practice the most informed medicine."

"In 2013, Venter told Bloomberg, "Genome design is going to be a key part of the future. That's why we need fast, cheap, accurate DNA synthesis so you can make a lot of iterations of something and test them." By then, he and his colleagues had already created a bacterial genome from scratch. Now, as the CEO and cofounder of Human Longevity, Inc., Venter hopes to combine information about various biological features—including the genome, proteome, biome and more—with advanced algorithms and computing to create new therapies to extend our years of high-quality life."
**NAGLA ABBALLAH**
head | Agricultural Genetic Engineering Research Institute
Cairo University | Giza, Egypt

A specialist participates in the science and use of genetically modified crops in a variety of crops. She is editor-in-chief of GM Crops and Food and the acting director of the Egypt Biotechnology Information Center.

**JULIAN ADAMS**
president | research & development
Infinite Technologies
Cambridge, Massachusetts, U.S.

With more than 30 years of experience as a chemist and executive in the pharmaceutical industry, Adams played a part in delivering many life-saving treatments. Among them was his role in the discovery and development of Velcade, a blockbuster cancer drug.

**RICH ALDRICH**
cofounder | Longwood Fund
Boston, Massachusetts, U.S.

A serial founder and builder of biotechnology companies, including Concert Pharmaceuticals and Vertex Pharmaceuticals, Aldrich repeatedly delivers capital to promising projects. His work, though, goes beyond biotechnology. For instance, he serves on the board of the Greater Boston YMCAs.

**MAHALETCHUMY ARUJANAN**
executive director | Malaysian Biotechnology Information Centre (MABIC)
| Selangor Dairi Ibni, Malaysia

When asked to identify a career-changing moment, Arujanan replied, “I was fired by one of my previous employers because I refused to play politics and apple polish the boss. I am who I am today because I left that employer. And the two most important traits I keep out of my organization are politics and the need to be ‘nice to the boss.’”

**SOL BAKER**
managing partner | SBJ Baker Consulting
Summit, New Jersey, U.S.

“We are optimistic that many fatal diseases can indeed not only be treated but potentially cured,” said Baker, former CEO and chairman at Genentech. Biotechnology “has impacted entrepreneurial behavior motivating students to go into this field, motivating entrepreneurs to create companies, encouraging investment in the field,” he added, “and all of this leading to better therapies for patients.”

**ANTHONY ATALA**
director | Wake Forest Institute for Regenerative Medicine
Winston-Salem, North Carolina, U.S.

“Atala declared at TED2011, ‘I aim to solve that healthcare crisis by making new organs with 3D printing, which could produce an unlimited supply for the patients who need them.’”

**DAVID BALTMORE**
Robert Andrews Millikan Professor of Biology | California Institute of Technology
Pasadena, California, U.S.

In his Nobel Lecture, Baltimore said, “The study of biology is partly an exercise in natural aesthetics. We derive much of our pleasure as biologists from the continuing realization of how economical, elegant and intelligent are the accidents of evolution that have been maintained by selection.”

**STÉPHANE BANCEL**
CEO | Moderna Therapeutics
Cambridge, Massachusetts, U.S.

After raising US$450 million for Moderna in 2015, Bancel told The New York Times, “We do not want to do what most biotechs do, which is one drug at a time. We want to go in parallel.”

**SETH BERKLEY**
CEO | Savi, the Vaccine Alliance
Geneva, Switzerland

“Even stronger public-private partnerships will ensure that the products of this revolution are made available to those living in the poorer parts of the world.”

**KAREN BERGENSTINE**
cofounder, chairman | editor-in-chief
BioCentury
Redwood City, California, U.S.

“Newspapers, movies and our culture in general are filled with uninformed views about science, business and economics that harm our society’s ability to make informed decisions about everything from food to medicine,” Bernstein says. “There is no simple fix for this, but I think we must try.”

**MARY BOOTE**
CEO | Truth About Trade and Technology
Des Moines, Iowa, U.S.

“Speaking specifically about agriculture,” Boote said, “the ability of a farmer to add a much-needed room to his home or pay a child’s school fees because of an increased yield due to biotech-crop access is a quality-of-life success story.”

**STÉPHANE BOUCHAR**
CEO | Burrill LLC
San Francisco Bay Area, California, U.S.

“Looking back on biotech’s history, Burrill opened, ‘On balance, the science has moved far faster than anyone could have assumed, and the business a little slower.’ 1,000 years from now when they write the then 3,000 years of recorded history of mankind, this will go down as mankind’s greatest moment—when we truly, for the first time, understood the basis of life and our ability to improve it, transforming health, agriculture, energy and industrial production.”

**ATUL BUTTE**
director | Institute of Computational Health Sciences | University of California, San Francisco, San Francisco, California, U.S.

“Discussing the new institute, Butte notes, ‘We hope that we will be successful in making discoveries and developing diagnostics and therapeutics. If we want to change the world of medicine, we have to bring those discoveries into the marketplace and closer to patients.’”

**BROOK BYERS**
founder member | Kleiner Perkins Caufield & Byers | Menlo Park, California, U.S.

Byers and his family support innovation so extensively at the University of California, San Francisco, that the school established the Byers Family Distinguished Professorship. Moreover, Byers is especially known for developing large venture capital funds devoted to biotechnology.

**BOB BRADWAY**
chairman and CEO | Amgen
Thousand Oaks, California, U.S.

Regarding a new manufacturing plant in Singapore, Bradley recently told the Pacific Coast Business Times, “This is an approach to manufacturing that we think will enable us to reduce our costs per gram of protein by an order of magnitude of about 60%.”

“People love innovation almost as much as they despise change,” Bobo said. “This aversion to change has delayed the adoption of agricultural biotechnology in some parts of the world. To increase the effectiveness of biotechnology, we need to build public support and trust. In order to do this, scientists need to stop telling people what they do and start telling them why they do it. It’s only after you build trust that science matters.”

**SCIENTIFIC AMERICAN | WORLDVIEW**

**“This aversion to change has delayed the adoption of agricultural biotechnology in some parts of the world.” —JACK BOBO**
That's what I did in between my high-wage jobs. “If not for his current saving medicines, but also high-value, enough high-quality scientists and the ethics of human and animal cloning and getting rejected by the NSF and NIH on the grounds that we did not understand the science and mammalian cloning was impossible.”

Ron Cohen, founder, president & CEO | Arcadia Therapeutics | Ardsley, New York, U.S.

To make biotechnology more effective, Cohen says, “I would start a $30 billion initiative to emphasize and improve STEM education in U.S. K–12 schools … We need to ensure that the next generation will produce enough high-quality scientists and industry leaders to maintain our leadership, which creates not only life-saving medicines, but also high-value, high-wage jobs.” If not for his current career in the industry, he would have been an actor in the New York theater. “That’s what I did in between my careers in medicine and biotechnology,” he said.

Peter Diamond, founder & chairman | XPRIZE Foundation | Sunnyvale, California, U.S.

In a 2012 interview with Wired, Diamond discussed, “If someone is always to blame, if every time something goes wrong someone has to be punished, people quickly stop taking risks. Without risks, there can’t be breakthroughs.” He won the XPRIZE with its mission of “designing and launching large incentive prizes to drive radical breakthroughs for the benefit of humanity.” Diamond is also co-founder of Craig Longevity, Inc., along with Craig Venter and Robert Hariri.

Susan Desmond-Hellman, CEO | Bill & Melinda Gates Foundation | Seattle, Washington, U.S.

Desmond-Hellman told Worldview that she wants to “accelerate a process” already underway at the Gates Foundation, which is “forging public-private partnerships to develop products specifically for the lowest-income countries.” She added, “In recent years, we’ve seen some very promising signs of what can happen when a nonprofit or a government agency works with a business to reduce market risks, such as through volume guarantees … If I could bring about any single change in the biotech field today, it would be to encourage all players in this sector to be more imaginative and aggressive about seeking such partnerships.”

Omid Farokhzad, associate professor | Harvard Medical School | Boston, Massachusetts, U.S.

Farokhzad said of one of his recent studies: “This is the first example of a targeted nanoparticle technology that reduces arterio- sclerosis in a mouse.” This work also explores nanomedicine’s potential to treat many other diseases.

Jenniffer Doudna, Li Ka Shing Chancellor’s Professor in Biomedical & Health Sciences | University of California | Berkeley, California, U.S.

One of the leading researchers who created the CRISPR-Cas9 technology for genome engineering, Doudna believes that we must “increase connections and communications among academia and companies” to help biotechnology move even farther ahead.

Michael J. Fox, founder | The Michael J. Fox Foundation for Parkinson’s Research | New York, New York, U.S.

Since 2000, Fox’s foundation has contributed over US$450 million for research on Parkinson’s disease, more than half of which went toward developing treatments. “We are outcomes-focused, incorporating milestones into every award and tying grant payments to achievements of those milestones,” the foundation website states.

Ronald Coven, founder, president & CEO | Acorda Therapeutics | Ardsley, New York, U.S.

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Russ Fraley, executive vice president and CTO | Monsanto | St. Louis, Missouri, U.S.

“From new areas of research in agricultural biologics to the intersection of science and precision agriculture, the seamless use of a variety of technologies—including biotechnology—will transform the future of agriculture.”


“When I was in college I made a commitment that I wanted to devote my life to service,” Greenwood recalls. “When I graduated, I worked as a house parent with special needs children, but I saw it as an opportunity to continue that focus on service,” he explained.
ROBERT HARIRI  
Chairman & Founder  
Celgene Corporation

"My greatest contribution has been my greatest blessing—my absolute passion for my life’s work," says Hart, who leads a biotechnology advocacy group in the biopharma legacy state of New Jersey. "Out of that has flowed an enduring optimism for the future, an unrelenting commitment to work hard for our members in their support of patients and an unquestionable belief that what we do matters."

WILLIAM HASLAM  
Chairman & President  
Access Health International

If Haseltine could make one change in the world of biotech, he would be "creating virtual biotechnology companies that outsource almost all aspects of clinical development, manufacturing and marketing of compounds sourced from academia. I would work with a small staff with little to no infrastructure."
“My philosophy has been one of differentiation. Look at what’s there and keep challenging yourself to be different.”

—KIRAN MAZUMDAR

KIRAN MAZUMDAR chairman & managing director
Bioncon | Bangalore, India

In the 2011 edition of the PwC Worldview, Mazumdar told us: “My philosophy has been one of differentiation, at most that which is new and keep challenging yourself to be different. If everyone is after generic products, how can you get into novel products, how can you get into novel products?”. For the most exciting application of biotechnology in the past year, Mazumdar said in the PwC 2015 US CEO Survey: “The stock prices of all biotechnology companies have increased dramatically in the past few years, so you hear talk about whether we’re in a bubble or not. I don’t think this is a bubble. These price increases reflect actual increased value and productivity in the higher number of drugs coming forward.”

TERRY McGUIRE cofounder & general partner | Polaris Partners | Boston, Massachusetts, U.S.

“IT’S not good enough to be intellectually smart,” McGuire once said, “you need to be clever, clever enough to figure out new ways to make things happen. Plus, you need ambition that is beyond monetary, a desire to see a better world.”

HENRY MILLER Robert Wesson Fellow in Scientific Philosophy & Public Policy Hoover Institution | Stanford University

Stanford, California, U.S.

Miller considers his most significant contribution to biotechnology to be “the record-setting approval of human insulin, when I headed the team that reviewed it in 1982.” He’d like to see more FDA advances today, including “more scientific, risk-based regulation.”

DAVID MOTT general partner | New Enterprise Associates Timonium, Maryland, U.S.

After executive roles in pharma, Mott moved to healthcare venture investing in 2009, where he quickly made a name for himself. In fact, FierceBiotech called him the “leading life sciences venture vanguard,” given the billions that he has raised.

KAREN NELSON president | J. Craig Venter Institute Rockville, Maryland, U.S.

Nelson’s group published the first paper on the human microbiome in 2006, which led to the establish of the Microbiome Center at The J. Craig Venter Institute. Her group also investigated an unbelievable awareness of the microbes in and on us! For the most exciting application of biotechnology in the past year, Nelson pointed to “Human Longevity, Inc.—bringing the genome, microbiome, metabolome and phenotypes of individuals, into a single vision with really major implications for how we approach healthcare.”

KIM POPOVITS chairman, CEO & president | Genomic Health | Redwood City, California, U.S.

“Defining the values of our company and the core focus of our company [are] centered around patients.” Popovits explained in a company video: “Each one of us who came here in the early days, I can say, was personally motivated—through professional or their own personal experience with cancer—to really transform cancer care.”

RICHARD POPS chairman & CEO | Alkermes | Dublin, Ireland

In 1979, Pops told Scientific American “Worldview” that even while jogging or playing tennis he lets “work run in the background. Sometimes the solution to some problem will arise after days and days. My philosophy of life is determined optimism. I am always able to turn adversity into opportunity.”

ROGER PERLMUTTER president | Merck Research Laboratories Boston, Massachusetts, U.S.

“I fairly early on established a pretty simple set of guiding principles,” Perlmutter told the American Association for the Advancement of Science in 2013, “Focus on grievous illness…focus on the task, not the tool…[and] do the experiment in people.”

GEORGE POSTE Del E. Webb Chair in Health Innovation biomedicine & biotechnology | Arizona State University | Tempe, Arizona, U.S.

Poste told us that he'd like to see “radical reform of NIH funding policies for academia,” adding, “Current NIH funding policies are anarchistic and propagate individual investigator-centric silos of reproductive biology, which is critically mass, and are ill-suited to address the complexity of unresolved disease challenges that require large scale, multi-disciplinary approaches, often involving multiple institutions.”

He also won the prize for the most embarrassing moment: “During my surgery training rotation at the University of Bristol Veterinary School in the UK, I quickly realized that I was ill-suited for a full-time career as a clinical veterinarian. Apart from angry patients who bit, kicked and scratched and were thoroughly respected the night was watched for my attempt to anesthetize a large tree porcupine from the zoo by applying the anesthesia mask to the wrong end of what was a large, swinging ball of spines, which prevented any easy effort to distinguish anterior and posterior axes.”

RAM SASESHERKARAN Alfred H. Capron Professor of Biological Engineering and Health Sciences & Technology | department of biological engineering MIT | Cambridge, Massachusetts, U.S.

Sasisekharan told us that his biggest contribution to biotechnology was “developing a technology platform for glycochemistry that has impacted both regulatory as well as drug development in various fields.” To enhance the effectiveness of biotech today, Sasisekharan would like find ways to “speed the process of bringing much-needed medicines to patients.”

LEONARD SCHLEIFER founder, president & CEO | Regenon
Tarrytown, New York, U.S.

“Of his early days as a bioentrepreneur, Schleifer recently told CNN, “We had this belief that the world needs innovative products.” But his career as a dealmaker began years before in the snow-shoveling business: “When you have to do a whole block’s worth of shoveling, you get a lot of experience” negotiating.”

AMY SCHULMAN venture partner | Polaris Partners Boston, Massachusetts, U.S.

Not afraid to laugh at herself, Schulman told The New York Times in a 2011 interview about the time she took a delegation: “I got there early, and I thought that the most important thing was to control the witness. I didn’t realize…when you control somebody it is not by intimidating them. But I adjusted the chair…so that he’d be really tall, and could look down impressively on the witness. But I realize as soon as I sat down, I toppled over and fell backward.”

RAMASWAMY RAVI distinguished fellow | School of Foreign Service | Georgetown University Washington, D.C., U.S.

With nearly 60,000 Twitter followers, Shah tweets on a range of topics, from coffee to Ebola. On February 18th he wrote: “We have to find new ways of bringing huge pools of capital to global health, especially in infrastructure. The day will come when we have to hold critical negotiations.”

PHILLIP SHARP institute professor | David H. Koch Institute for Integrative Cancer Research at MIT
Cambridge, Massachusetts, U.S.

“Many scientists in biotechnology are novel science and translation of this science to helping people through cofounding and participating on the boards of Biogen Inc. (1978) and Apylaim (2002).” Sharp said. “This has benefited millions of people around the world as patients and as well as the creation of new jobs.”

RAMSAY SASISEKARAN

KIRAN MAZUMDAR

KEVIN MOTT

KIM POPOVITS

RICHARD POPS

ROGER PEERMUTTER

GEORGE POSTE

RAM SASESHERKARAN

LEONARD SCHLEIFER

AMY SCHULMAN

RAMASWAMY RAVI

PHILLIP SHARP
people are in the iPSC field. The funding and infrastructure provided by the Japanese government is also a major factor, as these have encouraged excellent scientists to enter the field.

"Innovation in science and technology is at the heart of RegenBio's mission to discover and develop new treatments for serious diseases," Yancopoulos said while discussing the 2014 RegenBio Prize for Creative Innovation. "Investing in science education and the identification and development of talented new researchers is critical to foster tomorrow's medical breakthroughs."

At a conference in London, Zerhouni pointed out the urgent need for regulatory harmonization, saying, "In my short experience of five years at the FDA, I have not seen a single regulatory decision that was fully consistent across regulatory agencies."

"Our industry is very good at pattern recognition," Zohar told The WorldView. "However, creativity often involves breaking those patterns, doing things differently." She continued, "The ability to measure millions of physiological and other health-related data points over time is one of the most intriguing areas in terms of its impact on drug discovery, clinical trials and new medical modalities."
In 2009, Scientific American WorldView was launched to bring you the stories behind the numbers presented in our Scorecard of biotechnology innovation potential (page 36).

Since then, we have travelled the globe to discover the innovative technologies that are transforming our field and the lives of those who reap their benefits. Nonetheless, innovation also cannot build an industry. As Google cofounder Larry Page once said: “Invention is not enough. Tesla invented the electric power we use, but he struggled to get it out to people. You have to combine both things: invention and innovation focus, plus the company that can commercialize things and get them to people.”

Delivering cutting-edge biotechnology to people around the world requires a host of capabilities apart from simply having an innovative concept with great potential. This section delves into that journey “from bench to business” by meeting the researchers, mentors, CEOs, nonprofit leaders, venture capitalists and end users whose lives and livelihoods have been forever changed by it. (See “From Eureka to Useful,” page 3).

Then, a look inside LabCentral’s “launchpad” for life scientists, venture capitalists, and the corporate world that are using the lab to work toward commercialization—highlighting the excitement of a eureka moment and the right measures, feedback, foresight, and a persistent champion.

Developing an idea into a productive tool demands experience, foresight, and a persistent champion. BY MIKE MAY

or decades, a combination of politics and peer pressure pushed Eve Ntseoane away from farming in her native South Africa. Although her parents both grew up on farms, they couldn’t stay there as adults. “Black people were moved to townships, because of remnants of the Land Native Act of 1913,” she explains. During her time as a teacher, she only taught for three years before moving to the corporate world, where she worked in communications.

Nonetheless, her past and changing social circumstances eventually lured Ntseoane back to the corn fields. Through the South African government’s Land Reform Strategy, she obtained a 539-hectare farm south of Johannesburg. The plot is situated “near a little town called Vanderbijlpark, which is popular with genetically modified corn.”

In the early 1990s, Ntseoane recognized the potential impact of genetically modified corn. “At that time, I had to make a decision. Do I use the conventional methods, or do I rear more pigs and get a better return on my land? I faced the same decision, so I wasn’t able to make much.”

When the opportunity to research and develop genetically modified corn came about, Ntseoane jumped at the chance. “I like it to be based on breakthrough science that could be really game-changing.”

In South Africa, Eve Ntseoane more than doubled her yield with genetically modified corn.

Innovation is the creative lifeblood of every country. Langer explains that determining which innovations will lead to great products “depends a lot on your goal, because lots of things can be useful.”

“Like it to be based on breakthrough science that could be really game-changing.”

When assessing the way forward—from the discovery in the lab to working toward commercialization—“it’s important to learn from experience,” Langer says, “and have more capital rather than less.”

Also, Langer firmly believes that any innovation with a good chance of successful commercialization requires a dedicated, unyielding campaigner.

He watches many of his students take a dedicated, unyielding campaigner.

Making the right measures. The excitement of a eureka moment in the lab, however, can get some scientists moving too fast. “If the ambition is to commercialize an idea,” says Anders Nordström, a senior advisor at Sweden’s Uppsala Innovation Centre, "they are real champions of the ideas, and having a champion is very important." In fact, Langer gains empowering feedback for himself by watching his students advocate for their own ideas. “Having students do things that make them happy is very important to me,” he says.

Without a champion, even an amazing idea can fall flat. Langer often cites the Apple corporation as an example. With Steve Jobs and Steve Wozniak, Apple excelled. When the board decided to replace Jobs with a “professional” CEO, the organization stumbled through five of them while its business faltered. When Jobs took over again, it rose to become the world’s most valuable company. The lesson is, Langer stresses, is that even the most astounding innovators need the leadership of a champion to succeed.

BENCH TO BUSINESS
“many scientists focus too much on the technical science. They need to define what it means, the benefit, for the customer.” Which is not to say that potential buyers can always articulate their precise needs. “The market need might be there, but the customers might not know it yet,” he says. Just because something is a technical solution of some sort, however, doesn’t mean that a market exists for it or can even be created. To determine this, says Nordström, you “need to define the market and who will be the customer.”

For instance, Nordström describes an experience that he had with the Swedish Men’s Health Project, which was designed to help academic researchers commercialize their ideas. Olle Ericsson, then a researcher at Uppsala University, had a concept for a more efficient sample-preparation kit to be used in next generation sequencing (NGS). “Olle had no experience whatsoever in business, but was extremely eager to learn,” says Nordström, who was Ericsson’s mentor. He helped to get the project up and running.

The biggest mistake is thinking that your faith is fact.

Also, in terms of getting an innovation onto the market, projects must cross the so-called “Valley of Death”—that no man’s land where ideas or products to market also requires a highly-skilled workforce. “Being in an innovation hub like Boston,” Dudnik says, “it’s very clear that building human capability is absolutely critical to making the whole pipeline work.” (See “Biotechnology’s Crucial Question,” page 28.)

Many groups work together to build human capacity in the Nordic countries, which consistently rank high on the Scientific American Worldwide Scorecard. On this year’s list, for example, Denmark, Finland and Sweden placed second, sixth and eighth, respectively.

SCANDINAVIAN SUCCESS

To power innovation, the Scandinavian countries collaborate on many levels. For example, Sweden’s non-profit Uppsala BIO works to promote regional and national growth in the life sciences. Uppsala BIO’s CEO, Erik Forsberg, says, “We try to identify gaps in the system. What could make the life science sector grow more efficiently?” He answers part of his own question, saying, “It mostly comes down to innovation.”

Also, in terms of getting an innovation onto the market, projects must cross the so-called “Valley of Death”—that no man’s land where a concept is not far enough along to attract financial support but desperately needs it to move ahead. To increase the odds of crossing that divide, Uppsala BIO created the BIO-X program. “Here,” says Forsberg, “we can provide support through a network of competence—from users, such as clinicians, and from people with significant industrial experience. In addition, BIO-X can provide participants with a couple hundred thousand dollars for a couple years.” After that, says Forsberg, “You’ll need other funders.” The “other funders” in Sweden, and most other countries, provide venture capital (VC). To gain a better understanding of how biotechnology VC works in Sweden, Scientific American Worldview talked with Gunnar Steiner, CEO of Glimova Therapeutics in Stockholm and a venture partner for HealthCap, a family of VC funds investing in international life science research. In addition, Steiner has served as the CEO for several small biotech firms.

Although he admits his bias as a partner in a VC firm, Steiner says, “There would be no biotech industry if there were not a few in the field who would disagree with Steiner’s blunt assessment, because it takes money—often lots of it—to commercialize innovations. How VCs invest in biotechnology, though, depends on the overall economic environment, says Steiner. When the general economy is in decline, as in 2008, financing for biotech firms tends to dry up. This is a huge stumbling block for fledging innovators. “However, even when no one wants to invest in biotech,” he says, “there are always some companies seen as the best ones.” Those businesses are not very attractive. “But in troubled economic times, they’re the ones that get the VC. Such is the law of the VC jungle.

A key piece of support backed by exceptional science greatly improves the odds of getting funding to turn an innovation into a product, investors need to be convinced. “Bring as much data to the table as possible,” Steiner says. Impressive data, however, won’t always be enough to ensure that one particular eureka moment leads to a groundbreaking product that’s used around the globe, or anywhere, for that matter. Many other factors, from Niseoisa’s hard work on her farm in South Africa to Langer helping a student commercialize a research result—come into play in moving biotechnology forward. The best results emerge when great science is championed by an experienced team that lives and breathes persistence. Only then can biotechnology innovations change the world.
LabCentral gives start-ups the space and resources to thrive BY JOHANNES FRUEHAUF

n 2006, when Peter Parker and I started Cequent Pharmaceuticals, we needed a place to work, to do our science. There were loads of space options for tech companies that only needed a good computer and a high-speed Internet connection to launch a blockbuster, but few options for biotechnology companies like ours. We needed labs with sophisticated—meaning expensive—equipment, and the permitting, infrastructure and people to support it. Getting the right lab space setup took us six months and consumed precious resources, both human and financial, that we should have been spending on science. There had to be a better way.

In 2010, we started to believe that sharing could be the answer. We had just sold Cequent, and Peter and I both started new ventures—Bio-Innovation for Peter and Cambridge Bioslabs for me—at the Cambridge Innovation Center (CIC). At that facility, we thrived in the creative atmosphere of the shared space, and decided to try to adapt the co-working model into a shared laboratory environment for biotechnology.

Cambridge Bioslabs proved the concept that a biotech can get started on a small scale in a shared lab space. So Peter and I joined forces with Tim Rowe, CIC’s founder and CEO, to found a nonprofit called LabCentral. A US$5 million grant from the Massachusetts Life Sciences Center got us started, and we opened in late 2013 on Kendall Square.

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We quickly learned that Peter and I were not alone in thinking that start-ups in biotech needed LabCentral. In 14 months, 29 early-stage companies that work in the life sciences moved into LabCentral, and about 125 residents work here every day.

Upon moving in, the typical company consists of four people or less, most of them from academic institutions or teaching hospitals. To move forward with their technology, they have already secured the rights to the underlying intellectual property through an option or a license agreement. Many are repeat founders or CEOs with experience launching and growing life science ventures. Others are first-time entrepreneurs.

Having started working at LabCentral, companies may grow, adding headcount quickly. Because they have access to millions of dollars worth of the best lab equipment possible, they can perform experiments that they could never have dreamed of if they had to do it alone. What’s more, they can spend their capital and time on advancing their science rather than buying equipment or building infrastructure. This gives them the flexibility to morph their original vision into one with greater promise, to reach their milestones more quickly, and makes it more likely for them to succeed overall.

Although some might call LabCentral an incubator, we don’t want that word to be used to define us. It feels as though start-ups are fragile, needing life support to survive. The opposite is true for the companies we select to take residency here. So, we call ourselves a launchpad—speeding strong companies to take off. We accept only start-ups with the highest potential. In 2014 alone, our residents brought in more than US$200 million in venture capital and other sources of funding.

The result is an open floor plan with a very deliberate traffic flow pattern and transparent work, lab and play spaces that inspire collaboration and sharing. The common corridor gently insists that LabCentral’s residents see each other multiple times per day. Labs are strategically located in the middle, with offices and amenities at either end. A key to the flow is the café. Food and good coffee bring people out of their workspaces, encouraging engagement and interaction, as do regular “lunch and learns” programs, big-screen movie and sports-viewing parties, and social- and business-networking events.

FILLING A VOID

Biotech start-ups need lab space and resources to test out a concept and nurture early ideas. To do that, these budding companies usually need affordable, move-in-ready laboratory facilities. That’s just what LabCentral provides, and more. It gives emerging life science companies the bench space, equipment, infrastructure and services that they need for the early-stage research that is necessary to transition into commercial-stage enterprises.

Nonetheless, it’s the “more” that makes up LabCentral’s “secret sauce.” As the tech world figured out long ago, ideas expand when they can bump, mix and mingle with others; but this rarely occurs in life sciences start-ups, which typically set up in traditional lab settings with distinct and separate accommodations. Mingling happens every day at LabCentral, and deliberately. In fact, a push-me/pull-you exchange of ideas made up a primary requirement in our specifications for LabCentral’s design.

The result is an open floor plan with a very deliberate traffic flow pattern and transparent work, lab and play spaces that inspire collaboration and sharing.
CRUCIAL QUESTION

reality. Some might argue—myself
ogy and the people who turn it into
pendence of the underlying technol-
has been no progress. As true as that
28 SCIENTIFIC AMERICAN

BY STEPHEN M. SAMMUT

a difference in the
something that makes
od, cure, device or
Without a new meth-
likely: the technology.

the reflexive answer to

a category. Entrepreneurial enablers
some people who have a sub-
set of scientists, managers or a com-
bination of the two, it is best to break
them out into a separate category, becau-
se the risk affinity—or toler-
ance—of the entrepreneur is typically
the starting point of new venture cre-
ation in this industry and all others.
Entrepreneurs possess a combination
of innate skills, education, experience
and personality traits that put them
in a category of their own. Some are
aware early in their careers that en-
trepreneurship is their career destiny.
Others discover their inner-entre-
preneurial tendencies years after
commercial responsibilities that build
their confidence and hone their skills.
Entrepreneurial enablers.

Entrepreneurial founders.

Although these people put up a sub-
set of scientists, managers or a combi-
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their confidence and hone their skills.
Entrepreneurial enablers.

category. Entrepreneurial enablers are
the experienced managers of func-
tional areas—such as technol-
gy and information management,
strategy and marketing, finance and
operations—who have the risk toler-
ance and drive to make something
new happen, but who might not in-
dependently have the vision for a
new business. They know a talented
founder and leader when they see one
and a sound idea when they examine
one, but they see themselves as team
players and experts in their respec-
tive fields. Without the enablers, there
would still be entrepreneurs, but not
many of them would be successful.

ENTREPRENEURIAL EQUATIONS

What, then, does the biotechnology
industry need in the way of human
resources? To answer this, we can
look at the census of biotechnology
companies. According to a 2011
OECD (Organisation of Economic
Co-operation and Development)
study, the United States had the
largest number of biotechnology
firms—6,213—with the 18 reporting
countries from the European Union
having a total of 5,398. That’s about
11,500 firms before we start counting
Japan, Australia, New Zealand or the
emerging markets. For round numbers,
let’s stipulate that there are 15,000
companies globally in the industry.
How does that census translate
into people with entrepreneurial lean-
ings? It means there must be 15,000
entrepreneurial founders. If each com-
pany needs, say, six entrepreneurial
enablers, that would compute to a to-
tal of 90,000 of them worldwide. So,
overall, the industry requires 105,000
bio-entrepreneurs.

Beyond the numbers, these lead-
ers have to possess many capabilities:
Leadership: formulate human re-
source needs and manage the hiring
and development of teams.
Strategic thinking: make choices
based on alternatives and options.
Tactical planning: organize resourc-
es to achieve strategic ends.
Technology assessment: manage
a team that can review and
opportunities and select those that
justify a commercial strategy and
allocate resources proportional to the
opportunity.
Market assessment: recognize
and measure the potential of a technol-
driven product to meet unmet cus-
tomer and commercial needs, com-
pete with alternatives, achieve a level
of pricing that justifies the investment
and assures sustainability, and that
can be promoted with a clear, dis-
tinct, ethical and persuasive message.
Regulatory development: define
and manage the process through which
the products must be assessed.
Intellectual property management:
form, maintain and maximize intel-
lectual property assets internationally
domestically through a variety
of strategies, including licensing and
partnering.
Capital formation, replenishment
and stabilization: define capital re-
quirements and sources over long
periods, and allocate the fi-
nancial resources necessary to meet
the development and commercial ob-
jectives of the company.
Communication management: en-
capsulate the mission and methods of
the company into a succinct and
persuasive message in order to attract
human resources, build internal con-
sensus, drive strategy and operations
in an organized fashion, assure stake-
holders that the company is mindful of
the totality of challenges and ob-
tain needed financing.
Impact management: marshal the
assets and resources of the company
in pursuit of defined needs in an ethi-

cal manner that delivers the greatest
to the greatest number of people.
This knowledge comes from for-
mal training and experience. Al-
though it is unreasonable to expect
that an intensive approach to impart-
ading the associated insights would
ever compete with disciplined study
over years or the lessons associated
with making day-to-day and strategic
choices, teaching can be developed to
provide new entre-
preneurs and entre-
preneurial enablers

entrepreneurial enablers with

a toolbox for orienting their
thinking and laying a ground-
work for immediate action as
well as long-term study.

Teaching can be developed to
provide new entrepreneurs and
entrepreneurial enablers with

a toolbox for orienting their

thinking and laying a ground-
work for immediate action as
well as long-term study. Achieving
that, however, requires a conscious,
deliberate effort aimed at identifying
the needs of the industry vis-à-vis
the talents and expertise of people
willing to dedicate their careers to the
field. Those needs will change over
time, but like biology itself, education
and training will adapt. What matters
most in this industry is, therefore,
its people.

Stephen M. Sammut is a senior fellow
health care management at The Wharton
School of the University of Pennsylvania
in Philadelphia and developer of the
Biotechnology Entrepreneurship Boot Camp.
THE TRICKY SCIENCE OF COMMUNICATION

In the field of biotechnology, the communication of ideas is often complicated by the variety of players taking part in the conversation. Companies address consumers through internal mechanisms and the media. The media speaks to company representatives and members of the public. Trade groups also get involved on many levels. The web of people talking to each other gets tangled.

And often much more is at stake than merely the communication of an idea. Whether a start-up sinks or swims can be determined by people talking to each other gets tangled.

The story focused on Paolo Zamboni, an Italian vascular surgeon who claimed to have discovered the true cause of multiple sclerosis (MS). Although physicians have long con
tended that MS is an autoimmune disorder, Zamboni theorized that it is actually a disease triggered by narrowing of veins in the neck. He asserted that this vascular constric
tion created a build-up of iron that, in turn, set off the cascade of inflamma
tion and nerve degeneration that are the hallmarks of the disease. Zam
boni advocated a treatment similar to balloon angioplasty. He even tested
the surgical intervention on his MS-afflicted wife and, as the CTV docu
mentary displayed, her symptoms seemingly improved. The treat
ment, nicknamed the “liberation pro
cedure,” was touted as a miracle cure.

It was a powerful and emotional story, but flawed. The media coverage—based only on
the most preliminary of Zamboni’s findings—sprung “an over-enthu
siastic and inadvertent promotion of some shaky science,” André Picard, the
Globe and Mail journalist who authored the original newspaper
story on the procedure, wrote in RMC
Medical Ethics in February 2013.

After the initial reports made the
rounds on the Internet, the public started demanding that health au
thorities make the procedure avail
able in Canada. The media coverage snowballed, prompting the overpre
tected amount of political involve
ment in the allocation of research
funding. Federal and provincial
legislators pledged millions of dol
lars to support clinical studies. That
research, however, failed to confirm
Zamboni’s hypothesis. The liberation
procedure proved ineffective and pos
sibly dangerous.

Shortcomings of Social Media

The Zamboni escapade was not the
first time that a scientific claim hyped
in the media turned out to be wrong.
Thanks to the growing power of
social media, public campaigns built
around questionable healthcare re
porting might have an increasingly large influence on medical research
and healthcare.

According to Roger Chafe, a health
policy expert at Memorial University
of Newfoundland in St. John’s, the rise of Facebook, Twitter and other
social networks reinforces the im
portance of professional healthcare
journalism. After all, he says, reports from the mainstream media are often
the ones that get passed around—and
those same stories are more likely to influence key policymakers. “Without
the link to traditional media,” Chafe
says, social media “just doesn’t seem to
have the same kind of traction.”

Yet, according to Gary Swit
zer, founder of the watchdog website
HealthNewsReview, traditional media
sources are still routinely disemina
ting misleading health information.
Switzer and a team of researchers
looked at about 1,900 health-related
stories in medical devices or other interventions published by the
U.S. news organizations between 2006
and 2013. As Schwartz reported in
July 2014 in JAMA Internal Medicine,
most of the stories overplayed ben
efits, minimized harms and ignored
discussions of cost.

This kind of poor reporting can
have real-world consequences. For
example, after U.S. regulators issued
searchers about a slightly in
creased risk of suicidal thoughts and
behavior in young people who take
antidepressants, widespread media
coverage spurred a dramatic decline

The Zamboni escapade was not the
first time that a scientific claim hyped
in the media turned out to be wrong.
For a long time, industry has been seen as the bad guy,” says Seema Kumar, vice president of innovation, global health and policy communication at Johnson & Johnson in New Brunswick, New Jersey, “but a huge gap exists in covering this important translational research that goes on in industry and R&D.” She points out that industry science, which involves translating basic research into practical healthcare solutions, has “a huge impact on our health and wellbeing.” She also acknowledges a wealth of newsworthy science and technology stories transpiring in industry, she doesn’t see them getting covered, which disappoints her. “I’ve been feeling that we are not doing enough as a community to advocate for industry science communicators and the press corps—in talking about science in business and industry,” she says.

Improving this situation, Kumar explains, will require greater efforts from all members of the community. Science writers have to be better educated about how science and R&D work in the industry, and industry science communicators need to do more to engage with the science press corps. Accordingly, she urges everyone in industry healthcare communications to “be more welcoming, open and transparent.” She adds, “We have to spend time building relationships that engender trust and a sense of shared purpose.” In one such collaborative relationship, for example, Johnson & Johnson has made its clinical trial data available for the Yale University’s Open Data Access (YODA) Project. “When we announced this agreement,” says Kumar, “the response was unbelievably positive inside and outside of our company.”

Ultimately, this type of cooperative exchange will result in a deeper understanding of the work being done. “We absolutely can’t underestimate the importance of communication in science,” says Kumar. “The more we get to know and understand science communicators—can do to see how important science is to society, the more it will benefit all of us in building a scientific powerhouse, an innovative country.”

—MIKE MAY

The evolution of how people deal with risk is a popular social concept—dubbed the “risk society” by German sociologist Ulrich Beck—that has resulted in an environment today where new technologies are scrutinized more, and GM crops have been embroiled in controversy from their introduction. Such controversial subject matter requires specific handling in communications. The ongoing controversy shows how this has largely failed.

Following Failed Philosophies

In many cases, efforts to communicate about GM crops have followed a linear, educational, one-way delivery, focused mainly on technical elements of the science. Likewise, these efforts failed to discuss, or even acknowledge, broader interpretations of risk, such as psychological and social factors. Many of the messages focused on benefits to farmers and informing a “rational” debate. In the 1970s, however, Nobel laureate and Israeli-American psychologist Daniel Kahneman and his late colleague Amos Tversky showed that decision making about risk is neither purely rational nor purely “irrational.” Still, many biotechnology organizations employ a strategic and tactical mandate predicated on only “rational” thinking.

Some experts know that information cannot be the sole source of communication about GM crops to really get across the point. Recently, Paul Samuelson, Paul Samuelson and Peter Sandman, one of risk communication’s pioneers practitioners, calls this concern “outrage,” and it’s a powerful force that can escalate if not addressed. Moreover, outrage might even increase in the face of sound technical data, because the higher concerns are not addressed and these facts may conflict with deeply held cultural views and commitments.

Even Facts May Fail

Experts, including regulators, view risk as measurable hazard, the product of probability and magnitude. People facing the risks, however, tend to focus more on what commonly confuses them than the “technical” hazard itself. Peter Sandman, one of risk communication’s pioneers practitioners, calls this concern “outrage,” and it’s a powerful force that can escalate if not addressed. Moreover, outrage might even increase in the face of sound technical data, because the higher concerns are not addressed and these facts may conflict with deeply held cultural views and commitments.

Industry often shuns this higher level of the risk debate. Instead, industry tends to reformulate the issues in terms of technical expertise and experience. It’s where it is undoubtedly most comfortable. Simply put, facts about the risk are not what those with concerns need to hear to address their reservations.

Nonetheless, communications around GM crops continue to focus on the facts. The communicators have assumed that the public just needed more information, and that a better-informed public would be more inclined to accept biotechnology for what it is. Both research and experience, however, fail to support this so-called “deficit model” of communication. Although the first academic papers that questioned the “knowledge gap” hypothesis were published in 1996, only recently have the critics of the deficit model been gaining traction.

Seeking Solutions

Changing deficit-model approaches will require a better understanding of why people oppose the use of genetically modified organisms (GMOs) from the perspective of risk and trust. Public engagement—as a concerted exercise in understanding respect (based on shared values and interests), uncertainties and, critically, vulnerabilities—will be essential. Moving forward will require authentic communication that does not rely on public-relations strategies, such as propaganda and third-party techniques. It will require products that consumers personally benefit from and can control their exposure to. Furthermore, industry must make more concerted efforts to be trustworthy, and a major part of this will be to increase the perceptions of shared values and benevolence. Similarly, regulators must safeguard the public trust, especially in complex cases that often hinge around degrees of uncertainty.

Many factors need to be in place to make the acceptance of GM crops difficult. Nonetheless, communicators in biotechnology, especially in North America, need to learn to accept the need to address the cultural values that come into play in communicat- ing about GMOs. For example, GMO Answers—a U.S. industry initiative—is a first effort to be responsive to viewpoints in a direct and candid way. As this initiative is duplicated in other countries, cultural aspects of the communication process will need to be assimilated into the process. This could well be a first step toward the development of a cultural cogni- tion theory of risk communication for GM crops that aims to deeply as- similate cultural values into a process not aimed solely at acceptance, but aiming at putting people in the best possible position to make a decision consistent with their values and beliefs.

Science communicators should continually monitor social-science re- search to gain further insights into the groups with which we are communi- cating. As a result, we will learn to un- derstand existing and new concerns—not just about GMOs, but also about all areas of innovation. When there are no perceptions of risk, we should use the science of communication in the communication of science. If we do, some of the glaring problems with GMO communication might be addressed.
The irony of our modern era, where advances in genome, molecular diagnostics, targeted therapies and other major medical innovations on the horizon are helping to individualize and personalize treatments while revolutionizing entire categories of disease, is that all of these tools and solution providers are working as effectively and efficiently as they could. The stakeholder least able to take advantage of the progress of precision medicine is the patient. While patients may be informed, even empowered with medical information, they do not have any way to act upon the data they are hearing every possible avenue.

Cure Forward puts patients in the driver’s seat and gives them the ability to take advantage of every option of care available to them, activating ALL parts of the health ecosystem.

For Patients – Cure Forward aims to make science relevant, understandable and actionable for patients. The proprietary platform will enable patients to:
- Learn about diagnostic testing and clinical trials. This information will help them in dialogues with their doctor about ordering tumor-profiling and other tests that can provide better outcomes.
- Electronically retrieve their test results from diagnostic labs into their Cure Forward account. If their labels or results available digitally connect on the network, users will be able to enter results manually or send their report to Cure Forward for manual transcription.
- Read Gene Stories, magazine articles written by journalists to tell the story of each gene and describe its importance in cancer care. The stories are designed to make genomic findings understandable and memorable to ordinary people.
- Post their information to a clinical trial exchange, a marketplace where trial sponsors can see them for the duration of their post and then invite them to participate. This is the opposite of blind searches on the Internet.
- Interact with other patients on the platform. Patients will be matched to “tribes” who resemble them on molecular, clinical, personal, and demographic factors, or set up their own tribes. Within tribes, people will be able to ask and answer questions or share relevant information.

For Health Care Providers – As personalized and “precision” medicine approaches become increasingly available and relevant in managing genetic-related diseases like cancer, health care providers (HCPs) are facing the challenge of effectively describing test results to patients. This is especially difficult in a short office visit. The Cure Forward Gene Stories will be available to HCPs as teaching tools. Additionally, through a linking process in Cure Forward software, patients will be able to connect with their HCPs and cooperate on trial matching. HCPs will also be able to view the Cure Forward test directory to find tests that might be useful for their patients.

For Diagnostic Test Providers – Because patients, their families, and their physicians use Cure Forward to find tests that may be relevant to their care, Cure Forward is a potent marketing channel for diagnostic laboratories (DLPs). Cure Forward DLPs will have the distinction of being patient-friendly in their stance about patient access and use of their data. Patients inevitably have questions about their genomic test results. These are complex tests, often with many findings that are not readily understandable. Cure Forward can answer many of the basic questions that otherwise might be handled by the testing laboratory. Consumer-friendly results can be time consuming, and partnering with Cure Forward will help a laboratory focus its time and resources toward its main objectives of providing high quality testing and interpretation. A recent U.S. Health and Human Services rule stipulates that patients can access their diagnostic test results directly from the test provider. This rule, while progressive and potentially beneficial to the patient, can result in extra work for laboratories, who may not have systems in place for constructive delivery of test results. Cure Forward can be a constructive channel for results delivery, without added cost or time commitment from the DLP. Cure Forward does not charge its DLPs for this marketing presence and constructive results delivery.

For Clinical Trial Recruiters – Clinical research is where transformative therapies are born but it can take 2-3 years to fill a targeted trial, and more than half of trial sites fail to recruit a single eligible patient. Cure Forward offers a mechanism for patients to instantaneously make themselves visible to all recruiting trials that might suit them. Trial sponsors receive notifications when relevant patients post, and can then invite those patients to apply through the platform. Patients choose from their available invitations, and Cure Forward makes the introductions.

By applying a marketplace solution to the scientific problem, Cure Forward aims to increase patient participation in clinical research, to help individuals gain access to new therapies and to help new innovations get to market sooner for everyone else.

No money will ever change hands unless a trial recruiter has already experienced success recruiting through Cure Forward. That means fast, brief, precise, low-cost recruiting, and pay-for-performance economics. This is a new way to access clinical studies.

Cure Forward aims to make science relevant, understandable and actionable for patients. The proprietary platform will enable patients to:
- Learn about diagnostic testing and clinical trials. This information will help them in dialogues with their doctor about ordering tumor-profiling and other tests that can provide better outcomes.
- Electronically retrieve their test results from diagnostic labs into their Cure Forward account. If their labels or results available digitally connect on the network, users will be able to enter results manually or send their report to Cure Forward for manual transcription.
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The ultimate goal of our medical ecosystem is to identify the causes of disease and proceed with the most effective treatment as efficiently and quickly as possible. While the last two decades have seen the rise in more available sources of information through web hubs, new apps and other platforms, the task of assessing large amounts of information and acting intelligently on it can be daunting for patients, as well as other stakeholders in the system. The fear that one is wasting time while the disease progresses brings that gnawing feeling in the pit of the stomach. The worry that a brand new therapy or clinical trial that might offer hope could be unseen, uninformative or simply unknowable is a source of frustration and some- times hopelessness.

We all know too well, whether personally or through family members, the anguish of receiving a difficult diagnosis. Even in an era of boundless health information, digital connect- ivity and modern diagnostic tools, patients and their loved ones can feel powerless against the forces of their condition. Questions inevitably arise: “Am I doing EVERYTHING that can be done to combat my illness? Do I truly understand the molecular diagnosis and am I able to have a thorough discussion with my doctor?”

Thus it’s easy to see why the patient and the patient’s community setting are simply not visible to trial sponsors until they apply for entry, and too often those applications never even get seen. Cure Forward offers a mechanism for patients to instantaneously make themselves visible to all recruiting trials that might suit them. Trial sponsors receive notifica- tions when relevant patients post, and can then invite those patients to apply through the platform. Patients choose from their available invitations, and Cure Forward makes the introductions.

1. U.S. Health and Human Services rule stipulates that patients can access their diagnostic test results directly from the test provider. This rule, while progressive and potentially beneficial to the patient, can result in extra work for laboratories, who may not have systems in place for constructive delivery of test results. Cure Forward can be a constructive channel for results delivery, without added cost or time commitment from the DLP. Cure Forward does not charge its DLPs for this marketing presence and constructive results delivery.
POWER POINTS
Which places around the globe are powering the success of biotech today?

LOCATION, LOCATION, LOCATION.

As any real estate agent will tell you, where a piece of property lies is the key to its value. And when that property is a groundbreaking new medicine or a cutting-edge business model, where it is being developed is crucial to its success. As Scientific American Worldview enters its seventh year of tracking international trends in biotechnology innovation, we continue to refine our focus on which countries provide the best conditions for ensuring that that innovation will grow and thrive.

The 2015 Scorecard also examines the drivers of global investment. After so many years of reporting slow declines in the financial position of biotech firms around the world, data from our last Scorecard presented a clear indication of economic recovery. This year, we see even more evidence of bounce back, especially in one particular country.

Our Scorecard pinpoints the countries, communities and financial sources that enable innovation to flourish.
IP PROTECTION

Objective and perceived measurements can diverge considerably. "Intellectual property is the invisible infrastructure of innovation," writes Michael A. Gollin in Driving Innovation: Intellectual Property Strategies for a Dynamic World (Cambridge University Press, 2008). Nowhere is that statement more accurate than in the field of biosciences. The capital and time invested in a new drug can only be recouped through strong protection of domestic IP protection. For example, a company may be inclined to abandon a drug lead if it cannot find profit-enabling markets for it. In prior issues of Scientific American, we have also shown that the strength of a country's IP protection correlates with its concentration of clinical trials. Accordingly, IP protection can impact whether a nation's scientists and physicians even play a role in global drug development, and if drugs will be developed for locally pervasive conditions.

We measure IP protection both objectively and subjectively. "IP strength" is drawn from a study (Park, W.G. Research Policy 37, 761–766 (2008)) that calculates the unweighted sum of five measures: patentable inventions, membership in international treaties, duration of protection, enforcement mechanisms and restrictions (e.g., compulsory licensing). Recognizing that perceptions also influence investment decisions, we account for subjectivity with Schwab's "perceived IP protection" metric (Schwab, K. The Global Competitiveness Report, 2014–2015). This index was created using feedback from a global group of business leaders when asked about their perceptions of domestic IP protection.

Although the United States comes first in the objective measurement, "IP strength," Finland, Qatar and Japan take the lead when the "perceived IP protection" metric is added to the calculation.
Without question, a healthy biotech industry is acutely reliant on the robust community of highly trained individuals who envision, develop, and produce its products. Biotechnology firms require employees with advanced degrees in a variety of disciplines, while the industry overall is dependent on a pool of workers skilled in very specific technology—creating “brain drain” for their desire to stay in the United States, while a lower score means that more Ph.D. graduates expressed a “talent retention,” we used the percentage of United States doctoral recipients who did not intend to stay in the United States after earning a Ph.D. finds an opportunity to stay; the objective of this metric is to measure the sentiment to not repatriate, rather than the actual emigration rate. Even countries with high scores in other areas—including Denmark and Finland—suffer significant amounts of brain drain. Overall, the United States, New Zealand and the United Kingdom take the first three spots in the Education/Workforce category, in that order. Last year’s leader and second-place finisher—Luxembourg and Saudi Arabia, respectively—dropped to the fourth and seventh spots.

The Education/Workforce category consists of five components. “Post-secondary science graduates per capita” is calculated using UNESCO figures for graduates divided by the population according to the U.S. Census Bureau International Database. We also employed OECD figures for “Ph.D. graduates in the life sciences per capita” and “R&D personnel per thousand employment.” To assess “talent retention,” we used the percentage of a country’s doctoral recipients who did not intend to stay in the United States following graduation there, as reported by the U.S. National Science Foundation. A higher score in “talent retention” signifies that more people earn their Ph.D.s in the United States and then return home, while a lower score means that more Ph.D. graduates expressed a desire to stay in the United States, creating “brain drain” for their home countries. We recognize that not every person who wants to stay in the United States after earning a Ph.D. finds an opportunity to stay; the objective of this metric is to measure the sentiment to not repatriate, rather than the actual emigration rate. Even countries with high scores in other areas—including Denmark and Finland—suffer significant amounts of brain drain. Overall, the United States, New Zealand and the United Kingdom take the first three spots in the Education/Workforce category, in that order. Last year’s leader and second-place finisher—Luxembourg and Saudi Arabia, respectively—dropped to the fourth and seventh spots.

The Enterprise Support category has traditionally been a specific company of a specified size and refers, usually, to conducting business in a country’s largest city. The “biotechnology venture capital” component was created using measurements from the OECD. We employed an index based on an international survey (Schwab, K. The Global Competitiveness Report, 2014–2015) for the “venture capital availability” metric. The fourth component, “capital availability,” comes from the Milken Institute Capital Access Index. The front-runners in this category have traditionally been Hong Kong, Singapore and the United States, with active jockeying for the top ranks. Last year Hong Kong came first, followed by the United States and Singapore. This year Singapore leads, trailed by the United States and Hong Kong.
For the fourth year in a row, Finland conquers all when it comes to Foundations, those “nut and bolts” factors that allow science-based enterprises to function and flourish. Moreover, Finland has taken the top spot for five out of the seven years of the Scorecard’s history. That’s quite a record.

The Foundations metric represents the quality of a nation’s infrastructure as it relates to potential innovation in biotechnology. A company can’t succeed without a stable supply of electricity, efficient means of transportation and so on. Weaknesses in the Foundations category are particularly troublesome, as they represent problems that cannot be resolved quickly. For example, it can take years to build a new power plant, port or network of highways.


As in the Foundations category, Finland takes first place in Policy & Stability. The Nordic nations dominate this area, holding four of the top seven spots, with Finland in first. Sweden in fourth, Norway in fifth and Denmark in seventh. This revealing section of our Scorecard demonstrates the dramatic impact of policy and overall stability on a country’s innovation potential.

Data for Policy & Stability are drawn from the World Bank’s 2014 World Governance Indicators, which consist of “political stability and absence of violence/terrorism,” “government effectiveness,” “regulatory quality” and “rule of law.”

Perceptions that a government could be overthrown or destabilized are reflected in the “political stability and absence of violence/terrorism” metric. The “government effectiveness” component quantifies opinions on the quality of a nation’s public services, of its civil service and the degree of its independence from political pressures, and of its policy formulation and implementation—as well as the credibility of its government’s commitment to such policies. “Regulatory quality” examines impressions of the ability of a government to formulate and implement sound policies and regulations that permit and promote private sector development. Finally, the “rule of law” component provides perceptions of confidence in and adherence to the rules of society, such as enforcing contracts and property rights.

Edging out most of the Nordic countries in the Top 10 for this category, Singapore and New Zealand earn the second and third spots, respectively. The United States continues to place poorly, finishing 20th.
### 2015 SCIENTIFIC AMERICAN WORLDVIEW OVERALL CATEGORY SCORES

<table>
<thead>
<tr>
<th>OVERALL CATEGORY SCORES</th>
<th>[TD]</th>
<th>[TR]</th>
<th>[DE]</th>
<th>[AS]</th>
<th>[PH]</th>
<th>[BS]</th>
<th>[BE]</th>
<th>[PM]</th>
<th>[FO]</th>
<th>[PC]</th>
<th>[ST]</th>
<th>[BU]</th>
<th>[GT]</th>
<th>[AR]</th>
</tr>
</thead>
<tbody>
<tr>
<td>UNITED STATES</td>
<td>77.0</td>
<td>67.0</td>
<td>55.0</td>
<td>45.0</td>
<td>65.0</td>
<td>60.0</td>
<td>62.0</td>
<td>60.0</td>
<td>64.0</td>
<td>62.0</td>
<td>58.0</td>
<td>55.0</td>
<td>53.0</td>
<td>51.0</td>
</tr>
<tr>
<td>CANADA</td>
<td>74.0</td>
<td>62.0</td>
<td>50.0</td>
<td>40.0</td>
<td>61.0</td>
<td>55.0</td>
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<td>55.0</td>
<td>58.0</td>
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<td>50.0</td>
<td>47.0</td>
<td>47.0</td>
<td>45.0</td>
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<tr>
<td>JAPAN</td>
<td>73.0</td>
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<td>49.0</td>
<td>40.0</td>
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<td>55.0</td>
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<td>50.0</td>
<td>47.0</td>
<td>47.0</td>
<td>45.0</td>
</tr>
<tr>
<td>SOUTH KOREA</td>
<td>70.0</td>
<td>59.0</td>
<td>47.0</td>
<td>37.0</td>
<td>59.0</td>
<td>54.0</td>
<td>54.0</td>
<td>54.0</td>
<td>56.0</td>
<td>54.0</td>
<td>49.0</td>
<td>46.0</td>
<td>46.0</td>
<td>44.0</td>
</tr>
</tbody>
</table>

**Notes:**
- [TD] = Total得分
- [TR] = Total Ratio
- [DE] = Development
- [AS] = Assistance
- [PH] = Partnerships
- [BS] = Business Support
- [BE] = Brain Export
- [PM] = Political Stability
- [FO] = Political Influence
- [PC] = Public Capacities
- [ST] = Science Talent
- [BU] = Business Dynamics
- [GT] = Global Trade
- [AR] = Anti-Retraining

**2015 SCIENTIFIC AMERICAN WORLDVIEW OVERALL RANKING:**

<table>
<thead>
<tr>
<th>RANK</th>
<th>COUNTRY</th>
<th>OVERALL CATEGORY SCORE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>United States</td>
<td>77.0</td>
</tr>
<tr>
<td>2</td>
<td>Canada</td>
<td>74.0</td>
</tr>
<tr>
<td>3</td>
<td>Japan</td>
<td>73.0</td>
</tr>
<tr>
<td>4</td>
<td>South Korea</td>
<td>70.0</td>
</tr>
</tbody>
</table>

**Overall Score:**

The table’s color-coding helps to reveal the weaknesses of some high finishers and the strengths of certain countries with lower overall scores. For example, fifth-place South Korea ranks relatively well in Education/Workforce. As the data make clear, the top finishers overall tend to score respectably in each category. That stands to reason, as a healthy biotech sector is dependent on so many factors—from a diverse workforce skilled in both bench science and business acumen. As a result, one could say that South Korea has managed to take advantage of everything from the availability of capital to the access to ports.

---

**Component Scores:**

- **Business-friendly Environment (HISHER + BETTER):**...
- **Business Expenditures on R&D (% of GDP):**...
- **VC Availability:**...
- **Post-Secondary Science Graduates/Population:**...
- **Infrastructure Quality (roads, ports, electricity, etc.):**...
- **Entrepreneurship & Opportunity:**...
- **Political Stability & Absence of Violence/Terrorism:**...
- **Government Effectiveness:**...
- **Regulatory Quality:**...
- **Rule of Law:**...

**Our 2015 Scorecard ranks the bio-
technology innovation potential of 54 countries. A nation’s aggregate performance in each of the seven categories—Productivity, IP Protection, Enterprise Support, Intensity, Education/Workforce, Foundations, and Policy & Stability—yields the final score.**

For the complete Methods, see page 46. In brief, for each country the aver-
age of a category’s component scores (e.g., “IP strength” and “perceived IP protection”) provides the category score. A simple sum of the category scores generates the overall innovation score. We use normalization techniques that give each component and each category equal weight.

This table lists all 54 countries in top-to-bottom order based on their overall innovation scores. It also illustrates a nation’s rank in each category, showing the sub-score for each category color-coded on a coarse scale in comparison to other countries. As a result, the table offers a quick overview of the final results, an indication of a nation’s rough performance in each category and the opportunity to compare the numbers when desired. Because the score is composed of averages of available data, any gaps in the data, indicated as blanks in the table, do not affect the overall scores.

The United States remains at the top, extending its lead from last year over the second-place country. The next tier of finishers, however, is rather tightly packed. Second-place Denmark, for example, scored 13% higher than 10th-place Canada. And there was only a 22% difference in the overall score between the second and 20th-place holders, Luxembourg.
This Scorecard assesses 54 countries on their innovation potential in biotechnology through a meta-analysis. The analysis includes 27 components arranged in seven categories: Productivity, Intellectual Property (IP) Protection, Intensity, Enterprise Support, Education/Workforce, Foundations, and Policy & Stability. The table shows the components of each category and the sources of data.

For each component, countries are ranked on a scale from 0 to 10, with the lowest-ranked country scored as 0 and the highest-ranked one scored as 10. A nation’s score in a category is derived from the average of the available component scores—any gaps in the individual components were ignored in calculating the averages for each category.

The overall innovation score is a sum of the category averages, indexed to a score from 0 to 50. The normalization involved in calculating the category and overall scores considers each component and each category on equal weighting. In short, the Scorecard gives equal importance to all components.

### Scientific American Worldview Scorecard Methodology

<table>
<thead>
<tr>
<th>Category</th>
<th>Component</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Productivity</strong></td>
<td>public company revenues</td>
<td>Lawrence, S. &amp; Lähteenmäki, R. Nat. Biotechnol. 32, 626–632 (2016), and company disclosures</td>
</tr>
<tr>
<td></td>
<td>number of public companies</td>
<td>Lawrence, S. &amp; Lähteenmäki, R. Nat. Biotechnol. 32, 626–632 (2016), and company disclosures</td>
</tr>
<tr>
<td><strong>Intensity</strong></td>
<td>public companies per million population</td>
<td>Lawrence, S. &amp; Lähteenmäki, R. Nat. Biotechnol. 32, 626–632 (2016), company disclosures and U.S. Census Bureau International Database</td>
</tr>
<tr>
<td></td>
<td>biotech patents per total patents</td>
<td>Organisation for Economic Co-operation and Development</td>
</tr>
<tr>
<td></td>
<td>business expenditures on biotechnology R&amp;D</td>
<td>Organisation for Economic Co-operation and Development</td>
</tr>
<tr>
<td></td>
<td>value added of knowledge- and technology-intensive industries</td>
<td>U.S. National Science Foundation’s Science and Engineering Indicator</td>
</tr>
<tr>
<td></td>
<td>biotechnology venture capital</td>
<td>Organisation for Economic Co-operation and Development</td>
</tr>
<tr>
<td></td>
<td>capital availability</td>
<td>Milken Institute Capital Access Index</td>
</tr>
<tr>
<td><strong>Education/Workforce</strong></td>
<td>post-secondary science graduates per capita</td>
<td>UNESCO and U.S. Census Bureau International Database</td>
</tr>
<tr>
<td></td>
<td>Ph.D. graduates in the life sciences per capita</td>
<td>Organisation for Economic Co-operation and Development</td>
</tr>
<tr>
<td></td>
<td>R&amp;D personnel per thousand employment</td>
<td>Organisation for Economic Co-operation and Development</td>
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<tr>
<td></td>
<td>talent retention</td>
<td>U.S. National Science Foundation</td>
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<tr>
<td></td>
<td>brain drain</td>
<td>U.S. National Science Foundation</td>
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<tr>
<td><strong>Foundations</strong></td>
<td>R&amp;D business expenditures per GDP</td>
<td>Organisation for Economic Co-operation and Development</td>
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<td>government support of R&amp;D per GDP</td>
<td>UNESCO</td>
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<td>innovation &amp; entrepreneurship opportunity</td>
<td>2014 Legatum Prosperity Index</td>
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<td><strong>Policy &amp; Stability</strong></td>
<td>political stability &amp; absence of violence/terrorism</td>
<td>World Bank’s 2016 World Governance Indicators</td>
</tr>
<tr>
<td></td>
<td>government effectiveness</td>
<td>World Bank’s 2016 World Governance Indicators</td>
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<td></td>
<td>regulatory quality</td>
<td>World Bank’s 2016 World Governance Indicators</td>
</tr>
<tr>
<td></td>
<td>rule of law</td>
<td>World Bank’s 2016 World Governance Indicators</td>
</tr>
</tbody>
</table>
A SWAP AT THE TOP

Although Sweden dropped out of this year’s Top Five and New Zealand moved into third, the other four countries at the top—the United States, Denmark, Australia and Singapore—return as this year’s leaders, albeit jostled around a bit. There’s no change for the United States, which remained the front-runner since the launch of the Scorecard in 2009.

Some reshuffling took place among the other high-scorers. Denmark rose from third in 2014 to second this year. Singapore, on the other hand, dropped from second to third this year. Australia held its ground in fourth this year and last.

Perhaps 2016 will be the year the Philippines breaks free from the Bottom Five and begins to climb the Scorecard.

STAGNANT AT THE BOTTOM

The same five countries struggle

Last year’s Bottom Five nations are back again in 2015. Argentina took last place, with the Ukraine right above it, just as in 2014. The news might be even worse for Indonesia, which dropped from fifth in 2014 to third from the bottom this year.

Other countries in this group, however, did show progress. India rose one spot, from third from last in 2014 to fourth from last this year. The Philippines—now in its fourth straight year in the Bottom Five—also succeeded in moving up one place, to fifth from the bottom.

Despite the fact that the United States has maintained its top spot throughout, it is still interesting to observe the dynamics of the other highest-ranked countries. In early years, for example, New Zealand did not crack the Top 10, but in 2012 it ranked 9th and has stayed in the Top 10 ever since—breaking into the Top Five for the first time this year. Hong Kong may be following a similar path. Conversely, Canada started below the Top 10 in 2009, but in 2012 it ranked 9th and has stayed in the Top 10 ever since—breaking into the Top Five for the first time this year. In the future, we’ll be watching to see if Canada continues to straddle the line, or if it can hold onto its position in the Top 10.

These fluctuations in rank highlight important considerations in interpreting the Scorecard. First, the competition is fierce, and countries that do not invest in maintaining their positions may see others take their place. Second, the frequent movement makes it important to consider trends over time.

SEVEN YEARS OF BIOTECH TRACKING BY RANK

Our growing database reveals ongoing competition at many levels

Analyzing the Scorecard data from year to year uncovers certain trends, such as movement or stasis in the Top and Bottom Five, but a longer perspective shows much more. The end results demonstrate how each country changed relative to itself and others. Likewise, these data show the expanding list of countries assessed, although some lack data for every year.

Despite the fact that the United States has maintained its top spot throughout, it is still interesting to observe the dynamics of the other highest-ranked countries. In early years, for example, New Zealand did not crack the Top 10, but in 2012 it ranked 9th and has stayed in the Top 10 ever since—breaking into the Top Five for the first time this year. Hong Kong may be following a similar path. Conversely, Canada started below the Top 10 in 2009, but in 2012 it ranked 9th and has stayed in the Top 10 ever since—breaking into the Top Five for the first time this year. In the future, we’ll be watching to see if Canada continues to straddle the line, or if it can hold onto its position in the Top 10.
Most Leaders Lack Consistent Scores

Ongoing ups and downs plague many countries at the top

Some of the fiercest competition on the Scorecard is seen among the Top 10 countries. This graphic shows the volatility of their finishes by overall scores. Although the United States is consistently in first place, its overall score does fluctuate, even though it was nearly the same this year and last. Compared to the others in the Top 10, the United States earned fairly steady scores for 2009–2015: 37.1, 36.6, 39.0, 30.0, 39.6 and 39.6. That’s a seven-year average of 38.2, with the annual scores remaining fairly close to that number.

Going down the list, however, we see that all of the other Top 10 finishers have jumped up and down and back over the years. For example, Denmark’s scores for 2009–2015 were 31.4, 27.3, 31.9, 37.2, 35.7, 29.7 and 29.8. New Zealand’s scores move all over as well in that time: 30.0, 23.3, 24.9, 32.7, 28.6, 27.5 and 28.1.

So far, our growing database does not show any conclusive trends in scores at the top for any country except the United States.

Less Rocking in the Ranking

The order of the Top 10 countries varies less than the scores

In comparison to the overall scores, the ranking at the top looks relatively stable. It starts with the United States earning a steady first place across all years. Next, Denmark grabs the second-highest ranking over the life of the Scorecard—placing second four out of seven years. Sweden also earned relatively steady ranks over the years, always in the Top 10 and in the Top Five six of our seven years. Likewise, Singapore has secured a Top 10 ranking throughout the Scorecard’s history, never dropping lower than 8th place, and otherwise always reaching the Top Five.

Not every top-placing country, however, was so constant. New Zealand, for example, started in 7th in 2009, then dropped to 18th for two years, before getting back in the Top 10 in 2012 and staying there—moving all the way to 3rd in 2015. Hong Kong’s ranking leaps around as well: 17th in 2011, 13th in 2012, then 20th, 12th and 11th in 2013, 2014 and 2015, respectively. Like any industry, biotechnology demands ongoing efforts to maintain a nation’s standing on the world stage.
LARGE AND SMALL WINNERS, AND LOSERS

Countries of all sizes can be giants in their category

Freeman Dyson, now retired from his work as a physicist at the Institute for Advanced Study in Princeton, New Jersey, once said, “I see a bright future for the biotechnology industry when it follows the path of the computer industry, the path that von Neumann failed to foresee, becoming small and domesticated rather than big and centralized.” Maybe it’s a little early in the evolution of biotechnology to call it small and domesticated. Thus far, many parts of the industry remain big and centralized. Nonetheless, the leaders in the wide range of categories shown here hail from all around the globe, and they vary dramatically in size.

Small countries can be big players within a certain category. Take Qatar, for example. Not quite the size of the state of Connecticut, it is home to just a little over 2 million people, and its GDP is between the Gross State Products of Hawaii and New Mexico. Even so, it takes the gold medal in “greatest R&D personnel per total employment,” designating it as a highly educated, albeit undersized, nation.

Ranking first, though, is not always desirable. India, China and the Ukraine, for example, would surely prefer not to win the “worst brain drain” category, which means that they lead the world in the proportion of their students who would rather not return home after their Ph.D. studies abroad.

This map illustrates the state of biotechnology today, both in the tools that it requires and the places where it excels. Perhaps as time goes on, a map like this will look more and more like Dyson’s vision of “small and domesticated.”
AN AUSPICIOUS UPTICK
The U.S. sees an increase in public biotechs

Information from public companies—those whose shares are traded on public stock exchanges—provides a strong objective measurement of a country’s economic performance. Because they are publicly traded, public companies have greater transparency than private firms, and offer a clearer picture of a nation’s business landscape. We collect this information from a published study (Lawrence, S. & Lähteenmäki, R. Nat. Biotechnol. 32, 626–632 [2014]) and company disclosures.

For most of Scientific American Worldview’s history, the number of public companies has been falling around the world. As we’ve noted in the past, a decrease in public businesses should be considered in the context of other factors, such as employee counts, revenues or market capitalization. Increases in these other factors as company counts drop could indicate that the industry is consolidating, which can be a positive sign.

This year, the tally of U.S. public biotechnology companies increased for the first time in the history of Scientific American Worldview. Most other countries have seen a decrease in the number of public firms, although France has demonstrated a positive trend in this area since we started measuring in 2009. Understanding the complete story, however, also requires an analysis of the market capitalization.

CAPITAL GAINS
The United States takes its biggest lead yet in public-company market capitalization

One of the most telling metrics we use to chart the global biotech landscape is public-company market capitalization, or the market value of a business’s outstanding shares. When considered in combination with the number of public companies in each country, this information provides a broad international comparison of the industry. Our data on market capitalization was gathered from a published study (Lawrence, S., Lähteenmäki, R. Nat. Biotechnol. 32, 626–632 [2014]) and company disclosures.

The United States has historically led the world in biotech market capitalization, and continues to do so this year. But what’s striking is how much that lead has increased. A year ago, the U.S. market capitalization was close to four times that of the non-U.S. global total—and this year it ballooned to nearly six times that total. Australia had the second-largest growth, adding nearly US$5 billion in market capitalization, or roughly the sum of all of Sweden’s public biotechnology companies.

While most of the Top 10 countries saw progress in this area, Ireland was the lone standout, continuing its two-year drop.

The strong U.S. gains in both the number of public companies and public-company market capitalization indicate the likelihood of further growth ahead. In other nations, decreases in the number of firms, paired with increases in market capitalization, point to consolidation, which may help to support slower-growing domestic industries.
WHERE R&D IS DONE
A clear win for the U.S., and then it’s a tighter race

As we’ve noted in the past, countries promote domestic biotechnology industries for, among other things, the financial benefits of bringing in high-wage jobs associated with research and development. Accordingly, we take a look at where that R&D predominantly occurs.

Using data from a published study (Lawrence, S. & Lähteenmäki, R. Nat. Biotechnol. 32, 626–632 (2014)) and company disclosures, we present the simple sum of R&D expenditures in 23 nations. Here, the United States is the world leader—spending nearly 22 times as much as the United Kingdom, in second place. Then there is a near-tie between Australia, France, Switzerland and Denmark. Not surprisingly, these counties also rank high on market capitalization. This indicates that for many companies the bulk of their research and development is located in the same country as their headquarters.

US

MAKING R&D RELATIVE
Considering biotech spending in proportion to overall R&D reshuffles the rankings

In addition to assessing the simple sum of a nation’s R&D, we use the same sources to determine what proportion of its commercial R&D spending is dedicated to biotechnology. We report this as biotech R&D as a percentage of the business enterprise R&D expenditure, a metric that alters the country rankings derived from the simple sums.

In this relative measurement, Switzerland and Denmark take the lead, which is not surprising as they are comparatively small countries with strong biotech industries. Ireland’s position in third place, in the context of its relatively lower level of revenues, signifies that it is a desirable location for taking companies offshore.
THE SPENDING SPREAD BY SIZE

Big businesses outspend small ones in biotech R&D

Is Dyson’s vision about the future of biotechnology—that it may be heading toward an industry composed of small companies—taking shape? Our data may hold the answer. Using the OECD’s “Key Biotechnology Indicators” for October 2014, we collected information for 25 countries on the percentage of biotech R&D spent by small firms (meaning they have less than 50 employees) versus medium and large ones.

These data consist of public and private companies, making this analysis more inclusive than the public company figures presented earlier. For the majority of the countries considered here, large businesses accounted for most of the spending on biotech R&D. That was especially true in Denmark, the Netherlands and Switzerland, where large companies provided 94.6%, 92.1% and 90.9% of the spending.

Of all of the countries on this list, Israel was the only one in which small companies invested more in biotechnology R&D than medium and large ones. There, small companies supplied 67.1% of the spending.

Clearly, the numbers suggest that it will take some time before the biotech industry reaches Dyson’s predicted point.

THE SPENDING SPREAD BY APPLICATION

While biotechnology encompasses many sectors, the most investment is in healthcare

In addition to knowing the size of the companies engaged in biotech R&D spending, understanding the industry also requires an assessment of where the money goes. The United States and South Korea were not far behind, with large firms making up 88.4% and 87.7%.

In most countries there is significantly more R&D spending on health applications than on any other category. The second highest amounts spent were on industrial processing and agriculture. In the majority of cases, however, these areas received far less funding than healthcare. For example, in the United Kingdom 84% of R&D investment was on health applications. The United Kingdom’s next highest spending category: health, agriculture, food and beverages, natural resources, environment, industrial processing, and bioinformatics.
FOREIGN EXCHANGE
How host nations prosper from foreign direct investment

One of the many ways a country can improve its biotechnology business environment is through foreign direct investment (FDI), or when a person or organization controlling a company in one nation is from another. So if someone from France, for example, owns a business in Qatar, that would be considered FDI for Qatar. In this way, foreign capital and even expertise can flow to the host country, enhancing and expanding its domestic biotech industry. To examine the impact of FDI on various nations, we used a published study (Schwab, K. The Global Competitiveness Report, 2014–2015. World Economic Forum (2014)) and analyzed three metrics: prevalence of foreign ownership, business impact of rules on FDI, and FDI and technology transfer.

For the prevalence of foreign ownership metric—which is scored from extremely rare (1) to highly prevalent (7)—most of the countries received a 4 or higher. The top score, 6.3, went to Luxembourg, and the lowest, 3.0, to Kuwait. The business impact of rules on FDI assesses to what degree a nation’s business environment—its rules and regulations—encourages or discourages FDI. This metric is scaled from strongly discourages (1) to strongly encourages (7). According to our data, the rules and regulations in most countries encourage FDI. Ireland was ranked most encouraging, with a score of 6.6, which explains part of the reason it enjoys so much FDI. And even though Zimbabwe was saddled with the most discouraging score, 1.8, it still received a reasonable grade for the prevalence of FDI, suggesting that rules and regulations are not the only factors influencing foreign investment.

Without a doubt, these metrics add to Ireland’s appeal. It leads in “business expenditures on biotechnology R&D,” ties for second in FDI and leads business impact of rules on FDI. That combination cements Ireland’s position as a desirable location for foreign businesses to explore.

To measure how FDI can develop a nation’s biotech industry and increase its capabilities, we looked at the levels of new technology brought in by foreign investment. Using the same information source, we assigned scores from 1 (meaning FDI had no impact on bringing in new technology) to 7 (signifying it brought in new technology to a great extent) to each country. Not surprisingly, Ireland secured the highest score, 6.4. Most of the other countries also saw a significant amount of technology introduced through FDI. The lowest score, 3.1, went to Argentina.

Countries with strong technology flows gain a second benefit from FDI. In addition to the increased employment in domestic enterprises, this transfer of capabilities often seeds a new generation of homegrown tech-based companies.
Inventorship was assigned as the proportional representation of each country. For example, if a patent had two French inventors and one German one, then France would be given 66% credit for the patent, and Germany would receive 33%.

The results, from Inventor-Watch.com, show that the United States leads with 34,159 patents for 2004–2014. Japan, Germany and South Korea come in 2nd, 3rd and 4th with 6,236, 3,084 and 1,715 patents, respectively.

To measure biotechnology inventorship in the United States, we employed a similar approach to our global patent data (overleaf). This allowed us to pinpoint the centers of innovation in the country that produced—far and away—the most patents from 2004 to 2014. For this metric, we counted the number of patents from each state, based on the WIPO categories for biotechnology. Echoing the methods used in the analysis by country, for U.S. patents with inventors in a single state, we gave that state credit for one patent, regardless of the number of inventors. For patents with inventors in multiple states, inventorship was assigned as the proportional representation of each state. If, for instance, a patent had three Californian inventors and one from Connecticut, then California received 75% of the credit for the patent, and Connecticut 25%.

The results, available at InventorWatch.com, show California generated the most patents, 6,017—about 18% of the nation’s total. Massachusetts came in a distant second with 1,711, accounting for about 9%. Interestingly, every state in the union produced some patents, although North Dakota only obtained three in a decade.
As a meta-analysis, the Scientific American Worldview Scorecard is created from a broad collection of data comparisons. This year we added a new resource to this mix, the Nature Index (http://www.natureindex.com/), which tracks scientific publications. In past issues, we’ve examined the connection between a nation’s rank on the Scorecard and its publishing output, and the Index allows us to revisit that concept—but with data from a far greater number of countries. Our results show that several nations in particular generate many more publications than might be expected.

The Nature Index not only provides a database of scientific publications but it also keeps track of the institutional and country affiliations of each author. It divides articles in four main categories: chemistry, earth and environmental sciences, life sciences, and physical sciences. Data for each country are collected by article count (AC), with each nation receiving a credit for any article in which it can claim one of the authors. The database also calculates a weighted fractional count (WFC), which indicates the percentage of authorship from a country (and includes an adjustment that addresses an imbalance in some of the journals being tracked). For each country, we compare the Nature Index 2014 WFC for life sciences articles to the overall Scorecard ranking (excluding Hong Kong and Puerto Rico, which are not in the Nature Index). Not surprisingly, the results show considerable scatter, especially since some segments of the life sciences do not relate to biotechnology. Likewise, other categories of the Nature Index, such as chemistry, include articles that would impact aspects of biotechnology. Nonetheless, the graph shows that a higher overall Scorecard finish is associated with a higher article output. In fact, the findings suggest a potentially exponential correlation. Certain countries score much higher than expected. For example, the U.S. WFC lands near the top of the chart—more than four times greater than predicted by the correlation equation that best fits the data. China also exceeded expectations, publishing far more articles than other nations finishing as low as it does on the Scorecard. As we’ve noted in the past, however, publishing lots of articles is not the same as publishing lots of valuable articles.

Information from the Nature Index, a new database that tracks affiliations of high-quality scientific articles, enables us to generate an informal “collaboration metric” in peer-review publishing. Here, we present that metric for life sciences articles. The results show that countries ranking higher overall on the Scientific American Worldview Scorecard tend to collaborate less in terms of article authorship.

To make this calculation, we started with the Nature Index’s 2014 article count (AC) and weighted fractional count (WFC) for the life sciences category. Then we computed each nation’s percentage of collaboration, or how many of its articles included authors from other countries. (We calculated this metric as: \[(AC – WFC)/AC\] * 100.)

Much like the comparison of life sciences AC versus the overall Scorecard results, the data show considerable scatter. In general, though, an increase in the overall Scorecard ranking correlates with a lower rate of collaboration with foreign authors for life sciences articles.

Also like the previous comparison, some countries take the trend to an extreme. The United States, for example, earned a collaboration score of about 22%, while the trend would predict that number should be about 40%. This means that scientists in the United States collaborate with foreign authors far less than expected. The same can be said for India. Although it received a collaboration score of about 45%, according to the trend its score should be closer to 80%. Japan’s collaboration rate is also considerably lower than expected.

The take-home message seems to be that countries with less potential in biotechnology tend to collaborate more on articles. That could be a pragmatic result: they have no choice. However, keeping in mind Dyson’s vision for the future of biotechnology—as small and domesticated rather than big and centralized—it’s possible this trend may very well shift in the years ahead.

In any case, comparisons like these reveal the vast potential of combining the power of two rich databases. The articles that follow—“Products of Their Environment” (see page 66) and “Laws of Attraction” (see page 68)—offer additional examples of how pooling more data sources helps us to dig ever deeper into the complexities of this industry. (See more at www.natureindex.com.)
PRODUCTS OF THEIR ENVIRONMENT

How R&D location impacts which drugs are produced. By Yali Friedman

Where are drugs currently invented, and where will future drugs come from? A key question facing drug developers and policymakers is whether drug development will shift locations, in much the same way that manufacturing jobs and business administrative jobs have moved from industrialized to emerging economies.

Although the location of innovation might initially seem to affect primarily the economics of healthcare—reducing drug prices or increasing throughput of new drugs—it can also have qualitative implications. For knowledge-based activities, such as drug development, the scope of the research projects constrains the outputs. For example, strong research funding in Western countries may result in fewer drugs being developed for Western conditions, and more drugs being developed for previously neglected conditions.

WHERE ARE DRUGS INVENTED?

This study extends prior investigations (Friedman, Y. Nat. Rev. Drug Discov. 9, 835–836 (2010) and Friedman, Y. Nat. Biotechnol. 32, 523–524 (2014)) and goes further to examine patents covering marketed pharmaceuticals by leveraging objective drug-patent linkages. The logic is as follows: 1) The United States is the world's largest pharmaceutical market, so most—if not all—globally valuable drugs should have U.S. patents. (The primary purpose of this study is to compare innovation outside the United States, so any potential bias emerging from focusing on U.S. patents must be weighed against the benefits of leveraging rigid U.S. patent inventor listing rules and the objective drug-patent linkages provided by the U.S. Food and Drug Administration (FDA)); 2) For U.S. patents, all of the individuals who had “intellectual domination” of the research must be listed as inventors, along with their locations, and listing too many or too few inventors can yield a patent that is either unenforceable or invalid; 3) The FDA requires pharmaceutical manufacturers to submit a strictly defined list of patents covering the product and method of use of each of their drugs.

By consulting the DrugPatentWatch.com database and following this logical chain, I assembled a list of patent inventor locations from 2000 through 2014. To ensure that every patent was counted on par, each nation was attributed proportional ownership of each patent. For example, if a patent’s inventors are all from a single country, that country would get credit for one patent. For a hypothetical patent with two Swiss inventors and one German inventor, Switzerland would receive two-thirds credit and Germany one-third credit.

In the global continental distribution of drug patent inventors, North America—largely the United States—has maintained a roughly 50% representation, Europe about 30% and Asia approximately 10% (Figure 1). For all of the drug manufacturing occurring in Asia, there is little measurable innovation. The continued dominance of established pharmaceutical innovation hubs suggests that pharmaceutical innovation is very difficult to relocate. Just as Hollywood has maintained its position as the global hub of the television and movie industries, so too have the United States and Western European countries maintained their leadership in pharmaceuticals (data not shown).

When asked which nations in Asia are responsible for its drug inventorship, many propose that India or China might be the regional leader. A closer look at Asian countries demonstrates otherwise (Figure 2). Japan is the source of more than 90% of Asia’s drug patent inventors. Japan’s dominance in Asia further proves the permanence of pharmaceutical innovation hubs. Innovation has not moved in decades.

The continued dominance of established pharmaceutical innovation hubs suggests that pharmaceutical innovation is very difficult to relocate.

CHALLENGING CHINA’S ROLE

The lack of drug inventors in China and India challenges the emergence of domestic innovative capacity. With virtually no existing inventors in these countries, who will seed growth?

But, perhaps it is wrong to measure Asian innovation using the same metrics as for Western innovation. Innovation can differ substantially even among Western countries. For example, the MIT Production in the Innovation Economy (http://web.mit.edu/pie/) research group observed that innovative companies in the United States tend to emerge from new entities, but in Germany they are often built on legacies. So, using new company formation (i.e., the U.S. model) as a metric for innovation would create an unfair bias against Germany. The MIT group also noted that, contrary to popular opinion, Chinese firms excel in mass manufacturing “not because of low-cost labor, but because of their ability to move complex advanced product designs into production and commercialization.”

Accordingly, if Chinese innovation is based on process improvement, rather than low-cost labor or development of novel drugs, then one must ask: Why are China’s policies directed at Western objectives? Through directed incentives, China has established itself as a world leader in scientific publishing and in patent filings (as shown in previous issues of Scientific American Worldview). Low citation rates of scientific papers and low patent-grant rates demonstrate that these policies are not producing effective inputs for innovation.

In other words, China’s current strategy promotes Western-style outputs to anachronistically build foundations, rather than supporting its substantial capabilities already in place. A better development path would be to leverage China’s unique strengths in advanced manufacturing and design to improve on existing drugs and to develop global leadership in research in areas that other countries cannot address.

Yali Friedman is publisher of DrugPatentWatch.com, a competitive intelligence database focused on pharmaceutical patents.
How a nation’s policies attract and discourage biopharma investment

By Meir Perez Pugatch, David Torstensson, Rachel Chau, Amir Dayan & Noa Weinstein

C

iven the inherent challenges involved in the policymak-
ing process, not least when it comes to healthcare and biomedical innovation, the question is often asked whether policies actually matter. At the end of the day, does the state of the policy environment really translate into more or less investment and innovative activities in the biotech sector? The answer is yes.

A growing body of data shows that there is a positive link between country performance—based on the laws, regulations and initiatives in place affecting biopharmaceuticals—and its outputs, such as biomedical R&D and the production of new health technologies. In other words, whether or not a nation provides, for instance, support for basic research, strong biopharmaceutical-related intellectual property rights, robust regulatory standards, streamlined processes and a fair price does in fact impact its competitiveness and attract or repel biomedical investment much more than might initially be expected.

Such findings not only suggest that putting policies in place that support biomedical innovation is important if countries want to actually attract investment and improve the competitiveness of the local sector, but they also shed light on which areas nations might want to focus on in order to enhance their chances of securing investment.

ASK THE EXPERTS

One way of measuring the importance of policy inputs to investment, and identifying which are most important, is to poll those actually making investment decisions—for instance, local biopharmaceutical executives. Indeed, country managers and their team members have a candidate and an accurate understanding of how different aspects of the local policy environment factor in when discussing whether to allocate further resources in the nation. This is precisely what the Biopharmaceutical Competitiveness and Investment Survey (BCI)—a global survey-based index of countries’ biomedical-investment attractiveness—aims to understand.

First presented in the 2012 Scientific American Worldview (“Does your country deserve investment from biopharm?”), the BCI ranks nations’ biopharma investment environments based on the perspectives of local executives. The BCI is composed of 50 questions that capture the entire biopharmaceutical ecosystem, from scientific capabilities to market conditions. Using statistical analysis, respondents’ answers are translated into a quantitative score, which is used to benchmark countries’ performance and overall attractiveness for investment. The first edition covered 11 developed and emerging markets.

The second edition of the BCI, carried out in 2014, covers 16 nations. Among other insights, the 2014 BCI reveals a clear link between policy actions and levels of investment. Those countries with market-based, pro-innovation policies in place—such as the United States, United Kingdom and Switzerland—score at the top of the sample (Figure 1). In contrast, even considering their high levels of demand and future market potential, those markets that do not yet provide wide-ranging support for biomedical innovation—such as Brazil, Russia, India and China, the BRICs—still tend to place at the bottom of the group.

Take, for example, countries using protectionist-type policies or requirements to stimulate local biomedical manufacturing or R&D. The BCI results suggest that these and similar policies that seek to localize do not constitute part of a policy mix that attracts biomedical investment. Rather, nations that have introduced heavy-handed localization policies in the past few years, on top of not prioritizing policies that are also necessary conditions for biomedical innovation, tend to score poorly relative to other countries.

To illustrate, Russia has implement-
ed top-down policies, such as preferen-
tial treatment for domestic manufactur-
ers, to meet its Pharma 2020 goals of increasing locally produced medicines and growing export markets. Yet, these policies came prior to adequately ad-
dressing areas like quality of manufac-
turing and scientific capabilities and the soundness of its regulatory and legal frameworks. Not surprisingly, Russia scores below 60% of the total possible BCI score, and is categorized as “strug-
gling to compete.” Moreover, Russia is ranked lowest in the exact areas in which it seeks to be competitive, such as in manufacturing, where it scores well below the rest of the group at just 54% (Figure 2).

In general, policies that run contrary to the conditions needed for biomedical innovation are likely to translate into reduced biopharma investment. In addition, low costs, demand and market potential are not sufficient prerequisites for invest-
ment; rather, the policy environment is an equally, if not more, important determinant. Finally, the outputs themselves, or the lack thereof, actu-
ally shed light on which policy inputs are necessary to promote investment.

Ultimately, looking at the policies of countries that secure biopharma investment might provide a roadmap for all nations seeking the same success.

Meir Perez Pugatch is managing director of Pugatch Consilium and IPKM profes-
sor at the University of Maastricht. David Torstensson and Rachel Chau are partners, Amir Dayan is CEO, and Noa Weinstein is a statistician at Pugatch Consilium.

THE IP POLICY ENVIRONMENT IMPACTS INVESTMENT: ASSOCIATION BETWEEN THE LEVEL OF IP PROTECTION & CLINICAL TRIAL ACTIVITY

(IP’s impact)

Quantitative measures of actual levels of investment also confirm the maxim that policies matter. One area where this is remarkably clear is intellectual property (IP) protection and the effect of a country’s IP envi-
ronment on the number of clinical trials hosted in that country. As a proxy for biomedical foreign direct investment, we found that nations with weak IP environments, as mea-
sured by the U.S. Chamber of Com-
merce’s GIPC International IP Index (GIPC Index), tend to host three to five times fewer clinical trials than countries scoring in the upper half (Figure 3). In fact, regression analysis of the data suggests that the strength of IP protection can explain over 40% of clinical trial intensity, which is sig-
nificant given that a number of other factors—such as adequate capabilities and infrastructure—are also typically considered important for attracting clinical trials.

China makes an interesting exam-
pole. By some measurements China’s IP laws are considered as being well in terms of protection, but overall it continues to represent a very chal-

lenging environment, scoring in the bottom half of the countries sampled in the GIPC Index. Concurrently, China hosts a very small number of clinical trials in per capita terms—less than 1 trial per million population in a given year—which is among the lowest globally.

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**Table: BCI OVERALL SCORES & RANKING**

<table>
<thead>
<tr>
<th>Country</th>
<th>Overall Score</th>
</tr>
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<tbody>
<tr>
<td>USA</td>
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<td>BRAZIL</td>
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</table>

**Figure 1:** The second edition of the BCI, carried out in 2014, covers 16 nations.

**Figure 2:** By some measurements China’s IP laws are considered as being well in terms of protection, but overall it continues to represent a very challenging environment, scoring in the bottom half of the countries sampled in the GIPC Index. Concurrently, China hosts a very small number of clinical trials in per capita terms—less than 1 trial per million population in a given year—which is among the lowest globally.

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**Table: GIPC International IP index score as % or total score; life sciences indicators, 2014; Clinical trial activity (standard /million population), average rate 2009-2013 Expos.**

<table>
<thead>
<tr>
<th>Country</th>
<th>GIPC International IP index score</th>
<th>Clinical trial activity (standard /million population), average rate 2009-2013 Expos.</th>
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<tr>
<td>USA</td>
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**Figure 3:** Quantitative measures of actual levels of investment also confirm the maxim that policies matter. One area where this is remarkably clear is intellectual property (IP) protection and the effect of a country’s IP environment on the number of clinical trials hosted in that country.
PARTNER PROFILE

For more than 3 decades, life science innovator Dr. Raymond Woosley has revolutionized patient care by harnessing the power of collaboration.

Prescription drug use in America continues to rise, and while properly prescribed medications can have a markedly positive impact on patients’ well-being, incorrect or inappropriate use of medicines can also have devastating consequences for patients. Assessing and communicating those benefits and risks has been the life’s work of Dr. Raymond Woosley. Over the past thirty years, Dr. Woosley has matched his keen scientific acumen, vision and organizational skills, carving out new areas of consensus science capable of tackling the complexities in both the efficient development and safe use of life-saving medications. He has made the greatest impact on medical progress as the founder of CredibleMeds, a national network of Centers for Education and Research on Therapeutics (CERTs) launched by the federal Agency for Healthcare Research and Quality in 1999 following a ten-year campaign by Dr. Woosley to obtain Congressional legislation and funding for such programs. “There was a critical need for research that drug companies would normally not perform,” he explains, “and that the National Institutes of Health just doesn’t fund.” Of particular concern to Dr. Woosley was the potential for certain medications to induce sudden cardiac death (SCD). “My brother died of SCD in 1996 because his doctor, a well-trained and extremely capable physician, did not know that the heartburn medicine he had prescribed had the ability to cause sudden death.”

In 2000, Dr. Woosley moved his CERT from Georgetown University to the University of Arizona, where it became AZCERT and eventually CredibleMeds. Through its web portal, CredibleMeds gives clinicians, researchers and patients access to a robust and continuously updated list of drugs that are categorized by their risks for causing torsades de pointes (Tdp), the heart arrhythmia that can lead to sudden cardiac death.

Currently, Dr. Woosley is working under a contract with the U.S. Food and Drug Administration to establish collaborations that can incorporate the potentially life-saving information created by CredibleMeds into the systems that support healthcare decision-making. This work is also supported by grants from the Bert W. Martin Foundation and Oracle Health Sciences and made possible by a new partnership between CredibleMeds, Banner Health Systems and the University of Arizona College of Medicine – Phoenix.

“We have developed a system to analyze drug safety evidence that can fuel a ‘behind-the-scenes’ software program that we call the ‘Auto-Pilot,’” Dr. Woosley explains. “When a medicine is prescribed, all of the medical evidence about the safety of that medicine is combined in information found in the patient’s electronic medical record. From that analysis, the system provides valuable guidance to the patient’s healthcare team.” (See sidebar.) Parallel to the development of CredibleMeds is the continued growth of the Clinical Path Institute (C-Path), which Dr. Woosley founded in 2005 in response to the need for collaborations that can incorporate those benefits and risks has been the life’s work of Dr. Raymond Woosley. Over the past thirty years, Dr. Woosley has matched his keen scientific acumen, vision and organizational skills, carving out new areas of consensus science capable of tackling the complexities in both the efficient development and safe use of life-saving medications. He has made the greatest impact on medical progress as the founder of CredibleMeds, a national network of Centers for Education and Research on Therapeutics (CERTs) launched by the federal Agency for Healthcare Research and Quality in 1999 following a ten-year campaign by Dr. Woosley to obtain Congressional legislation and funding for such programs. “There was a critical need for research that drug companies would normally not perform,” he explains, “and that the National Institutes of Health just doesn’t fund.” Of particular concern to Dr. Woosley was the potential for certain medications to induce sudden cardiac death (SCD). “My brother died of SCD in 1996 because his doctor, a well-trained and extremely capable physician, did not know that the heartburn medicine he had prescribed had the ability to cause sudden death.”

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PRESCRIBING WITH A MEDICATION SAFETY AUTO-PILOT:
An actionable, attainable step towards truly personalized medicine is the “Auto-Pilot” system envisioned by Dr. Raymond Woosley and being developed under AZCERT’s contract with the FDA’s Safe Use Initiative. The Auto-Pilot considers multiple factors in real time and provides the doctor and other healthcare providers with the most pertinent data needed to guide prescription therapy.

PHYSICIAN:
- Makes the diagnosis for a patient’s illness and chooses a prescription medication

AUTO-PILOT:
- Accesses patient data, including current prescription medications and their risk, allergies, other medicines and existing conditions
- Cross-references patient data against the continuously updated CredibleMeds list of drugs
- Determines potential drug-drug interactions or side effects that could harm the patient and displays the findings
- Confirms physician’s prescribed medication, or recommends monitoring or safe alternative(s)

Below is an illustration of how the Auto-Pilot would guide decisions for a prescription for Azithromycin:

Prescription for Azithromycin

Accept Medical Indication

Tdp Risk Score Positive

ECG Screen

Concomitant Tdp Risk Drug

Dispense Azithromycin

Dispense Azithromycin with QT monitoring

Suggest Safe Alternative

PHYSICIAN:
- Directs therapy and provides learning on how information received can be made more useful or improved

Food and Drug Administration’s Critical Path Initiative—an effort to accelerate the drug development and regulatory process.

C-Path’s mission entails reaching across the boundaries separating drug companies, academia, researchers, and regulatory agencies to facilitate unique cross-disciplinary collaborations, which take place in neutral, pre-competitive space. In its ten-year existence, C-Path has helped to improve the efficiency and efficacy of drug development by discovering and receiving regulatory endorsement for standardized biomarkers (tools to help speed drug development) for Alzheimer’s disease, Parkinson’s disease, skeletal muscle injury, kidney injury, and more. C-Path was also the first organization to effectively pool patient-level data from multiple clinical trials shared by several major pharmaceutical companies in order to better understand the course of Alzheimer’s disease. This database is now being used to design and simulate new clinical trials with greater likelihood of success in testing new treatments for this and other diseases.

“Today, digital and cloud technologies allow us the ability to analyze and communicate vast amounts of information in an instant,” Dr. Woosley says. “And while we’re doing that, C-Path is continuing to work to facilitate unique cross-disciplinary collaborations, which take place in neutral, pre-competitive space. In its ten-year existence, C-Path has helped to improve the efficiency and efficacy of drug development by discovering and receiving regulatory endorsement for standardized biomarkers (tools to help speed drug development) for Alzheimer’s disease, Parkinson’s disease, skeletal muscle injury, kidney injury, and more. C-Path was also the first organization to effectively pool patient-level data from multiple clinical trials shared by several major pharmaceutical companies in order to better understand the course of Alzheimer’s disease. This database is now being used to design and simulate new clinical trials with greater likelihood of success in testing new treatments for this and other diseases.”

“I think the tools and infrastructure now exist to enable research and healthcare delivery systems to fully utilize the enormous amount of data and knowledge our scientists are generating. But, partnerships such as those created by CredibleMeds and C-Path will continue to be essential for patients to reap maximum benefit from this investment in science. Future advances will require collaborations among translational scientists, those who deliver healthcare and those who train healthcare practitioners.”

Azithromycin

Makes the diagnosis for a patient’s illness and chooses a prescription medication

Accept Medical Indication

Tdp Risk Score Positive

ECG Screen

Concomitant Tdp Risk Drug

Dispense Azithromycin

Dispense Azithromycin with QT monitoring

Suggest Safe Alternative

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An Evening with Top Medical Innovators

Today’s visionaries battle cancer with cutting-edge science and the stubbornness to make it work
BY MIKE MAY | Illustrations by MEEN CHOI

 Surviving cancer requires teamwork. On the evening of Monday, December 8, 2014, a small army of some of the best “soldiers” in the battle against blood cancer mingled with patients and members of the press in “The Swamp” at the California Academy of Sciences in San Francisco. Just feet away, Claude—an albino alligator—laid still, but deadly, much like an undiagnosed cancer waiting to unleash itself. The crowd gathered there that night to learn how sophisticated research from dedicated scientists promises to—and in some cases already does—cure cancer.

This Top Medical Innovators forum was organized through a partnership between Scientific American Worldview and The Center for Medicine in the Public Interest (CMPI). The event recognized eight experts for their work in the fight against blood cancer, from diagnosis to treatment (see “Innovator Alley”). Gaining ground in this difficult battle demands crusaders like these to continue the mission of developing innovative new treatments.

As Jeremy A. Abbate—publishing director of Scientific American Worldview and global vice president for global media alliances at Scientific American—said in his introduction, “One of the most defining characteristics of the enterprise of innovating is taking nature and making it a little bit better, using what nature gives us and tweaking it just a little bit.”

Indeed, when a researcher’s discovery yields a revolutionary new medicine, that tweaking can change lives. “Innovation is inventiveness put to good use,” Bob Goldberg, one of the cofounders of CMPI, told the audience. “Inventiveness springs from the imagination of our honorees this evening.”

As I took the podium, I started to call up four of the innovators who joined us that night: Patricia Ernst of the University of Coloradoan Denver-Anschutz Medical Campus; Bob Hariri of Celgene Cellular Therapeutics; Carl June of the University of Pennsylvania’s Perelman School of Medicine; and Diane Wuest, representing Colin Hill of GNS Healthcare. I felt awed to be there as I invited Carl June to the panel.

CHANGING THE ODDS

June’s groundbreaking approach to combating leukemia begins with the immune-system cells from a particular patient, genetically re-engines those cells to kill that person’s specific cancer and then injects them back into that individual. He first used this protocol in 2010 to treat an adult with the disease—which typically kills 80–90% of its victims—and the injected cells destroyed seven pounds of tumor. The man is alive and well today.

In addition, June had recently completed a study in which 39 children with leukemia—for whom several traditional treatments had failed—received their own re-engineered immune cells. Of these children, 35 went into complete remission. That translates into a response rate of 92%! As June said, “It’s a heartwarming story, because you see kids who have gone through all the kinds of things that chemotherapy can do, or radiation, and most of them already relapsed after a bone marrow transplant—but after immunotherapy, these kids have returned to a normal life.”

MINING NEW TARGETS

Genetic solutions to cancer have been anticipated since the sequencing of the human genome more than a decade ago, and some of today’s treatments do target changes in genes. But Patricia Ernst believes that examining other cellular alterations will unveil even more targets. She looks at so-called epigenetics.

“Most people are familiar with the concept when you get cancer—one of your genes has suffered a mutation and that’s why the cells grow uncontrollably,” Ernst explained, “but there are a lot of other things that can happen to a cell.” For example, the molecules that control genes—known as regulators—may also cause or affect the growth of cancer. This is an example of epigenetics, and such changes can impact the onset and severity of leukemia.

“There are many new drugs that are being developed that not only influence heritable changes in gene expression,” she continued, “but also directly target epigenetic regulators that are mutated in particular leukemias.”

NEVER GIVE UP!

At Celgene Cellular Therapeutics, Hariri and his colleagues convert stem cells into new therapies for diseases including cancer.

As I thought over what the panel had said that night and looked over the crowd, I felt moved, too, and optimistic about a more powerful today and an even more innovative tomorrow.
Here are our innovators changing lives, and is sure to affect many more in the future. Eight “Top Medical Innovators” of the Public Interest recognized by the Center for Medicine in the Public Interest. Allison showed that blocking CTLA-4 on T cells can cause them to fight cancer more effectively, and this work led to the drug sipili-mumab, which is FDA-approved to treat metastatic melanoma.

IANNIS AIFANTIS, Professor and Chair of Pathology at the University of Texas Southwestern Medical Center, Dallas, Texas. Aifantis works on life science or medical research that is already changing lives, and is sure to affect many more in the future. Here are our innovators.

PATIENT CASE STUDIES: Innovation In Action

Iannis Aifantis

Professor and Chair of Pathology
New York University School of Medicine
New York, New York

Aifantis uses blood stem cells to study cellular development and how cells turn into leukemia and lymphoma. He also studies the immediate environment around a tumor in hopes of creating more targeted drugs.

Susan Desmond-Hellmann

CEO
Bill & Melinda Gates Foundation
Seattle, Washington

When Desmond-Hellmann was president of product development at Genentech, she contributed to the development of Avastin and Herceptin, which were two of the first gene-targeted therapies for cancer.

Patricia Ernst

Professor
University of Colorado Denver-Aschutz Medical Campus
Aurora, Colorado

Ernst studies the epigenetic—traits that can be inherited but are not in the genes—mechanisms that impact the development of healthy blood and the changes that lead to leukemia. This basic research uncovers a vast collection of new drug targets.

Bob Hariri

Chairman
Cellgene Cellular Therapeutics
Warran, New Jersey

Hariri discovered pluripotent stem cells, which are capable of developing into any kind of cell, within the placenta and pioneered their use in regenerative medicine. He and his colleagues work with these cells to fight inflammatory diseases, cancer and other conditions.

Colin Hill

CEO and Co-founder
GNS Healthcare
Cambridge, Massachusetts

Hill uses advanced computing, sophisticated algorithms and large datasets to assess the impact of drugs on patients. In this way, he is redesigning the manner in which we test drugs: instead of running clinical trials in humans, he runs clinical trials on computers.

Carl June

Professor in Immunotherapy
Department of Pathology
University of Texas at Austin

June developed CTL019 immunotherapy for B-cell cancers, including acute lymphoblastic leukemia (ALL), non-Hodgkin lymphoma and chronic lymphocytic leukemia. The US Food and Drug Administration gave CTL019 “breakthrough therapy” status in 2014 for the treatment of relapsed and refractory adult and pediatric ALL.

Christof Von Kalle

Director of Translational Oncology
National Center for Tumor Diseases and German Cancer Research Center Heidelberg, Germany

Von Kalle researches techniques in therapeutic genetics, such as using a virus to deliver a drug. This process could lead to treatments for certain cancers and the prevention of others. He also works with colleagues on new ways to diagnose cancer sooner and more accurately.

In February, several weeks before he planned to run his 86th marathon, Don Wright made time to talk with Scientific American Worldview. A few years earlier, in December 2012, he had achieved his goal of finishing one marathon in each of the 50 states. Now, he wants to raise his marathon count to 100, a feat he hopes to reach by the end of 2016. But without a doubt, his greatest accomplishment is staying healthy despite being diagnosed with multiple myeloma just after his first marathon, in 2003.

Then, instead of giving in to the cancer, he decided to take on the Boston Marathon, followed by one race after another. His wife and daughter often come along and run the half marathon at the events he attends. Wright can keep running in spite of his myeloma because of a once-a-day pill. He has been on the drug for seven years—starting with a clinical trial five years before it was approved—without any major side effects. Well, except for one, he laughs: “The big side effect is that it makes me want to go run marathons!”

Jokes aside, Wright deeply appreciates his treatment as well as his health. And of his current cancer-fighting medication, he says, “It’s helped me live long enough to meet my grandchildren, and that’s extremely important in my life.”

Marathon Man

72-year-old Don Wright—a multiple myeloma survivor—takes aim at his 100th marathon

Hardy Jones fights to protect marine life even as he battles cancer

In 2000, life couldn’t have been better for lifelong diver and filmmaker Hardy Jones. Teaming up with actor Ted Danson, Jones founded BlueVoice.org to protect whales and dolphins. But in 2003, he was diagnosed with multiple myeloma. His treatment started with an oral cancer medication and a steroid, which stops the growth of cancer cells in the bone marrow. “My myeloma burden was reduced by 97%,” Jones says. “It was very fast.”

He started on high doses of the medications, but his oncologist brought them down over time. Eventually, Jones got 16 months off without any treatment at all. “In that 16 months,” he says, “I was quite stable, but then the myeloma began to creep up.” So he tried another drug and experienced a similar cycle—treatment, quick cancer killer, then, eventual treatment vacation, followed by cancer recurrence, which led to a new treatment.

At 71 years old, Jones continues to receive treatment and pursue his work. When he spoke with Scientific American Worldview, he was deep in a project to save dolphins being killed in Peru for use as shark bait. “We’re making a film on it now,” he says. “If we don’t stop this dreadful practice, they will wipe out the dolphins and sharks.”

While Jones saves the world’s marine life, advanced drugs—with ongoing innovations keeping his options coming—save him. There is no better teamwork than that.
P

attention is a necessity for pharmaceutical companies seeking to bring drugs to market in China. Last year, to eight-year drug lag these firms have had to contend with was lengthened another two years. “A lot of products were asked to come in the last time to get the approval for clinical trial stage,” says Joseph Cho, who heads RDPAC, an association of 40 multinational R&D-based pharmaceutical companies working in China. The extension was unexpected. “We say it is a shock, not a surprise,” he relates.

Since being recognized in 2005 as a nonprofit by the Chinese government, RDPAC has developed into a lobbying voice for improving China’s pharmaceutical R&D environment. According to its website, the organization is “committed to securing patients timely access to innovative drugs”—a formidable task, particularly in China. As of early January 2015, the group reports that at least 34 applications from multinational drug companies have been delayed by a new step in the drug-approval process. And in addition to these global firms, says Cho, “The domestic companies who are focusing on their own R&D products are facing the same challenges.”

RDPAC is working hard for change, but has had limited success so far. The real challenge is getting the ear of the right high-level decision makers. “Policy making in China is so fragmented, so we are facing different ministries and sometimes they come up with different ideas about how things should be done,” says Cho. At RDPAC’s March 2014 meeting with China’s State Food and Drug Administration (CFDA), officials revealed the government’s rationale for the added two years. “They think they have been making mistakes in the past, and they just want to do the right things,” he explains.

Last year, the six-to-eight-year drug lag these firms have had to contend with was lengthened another two years.

Last year, China’s CFDA announced the recruitment of 20 new Center for Drug Evaluation employees, adding to its existing staff of 80 overworked reviewers, and earlier this year they announced the addition of 53 reviewers. In May, CFDA deputy head Yin Li announced plans to outsource some of the reviewing to third-party organizations. Even so, its capabilities don’t compare to the FDAs in other countries like the United States. As the agency struggles to get through the backlog of approvals and pick up the pace, Cho says foreign pharmaceutical companies are increasingly frustrated. “I think the sudden change of practice is making the lives of our R&D people and regulatory people on the ground and at headquarters frustrating. A lot of investments are being affected by these uncertainties here in China.”

Seeds of Controversy

German research provides clarity in the ongoing crop debate

Despite numerous scientific studies demonstrating the benefits and risks of genetically modified (GM) crops, they continue to be the subject of vehement debate. Low levels of public trust regarding GM crop safety present a major problem for experts and governments, as the demand for technological advances focused on food security has never been more pressing. Seeing a need for an objective breakdown of the facts, Martin Qaim, an agricultural economist at the University of Göttingen, Germany, and his colleague Wilhelm Kümper conducted a meta-analysis on the effects of GM crops on pesticide use, crop yields and farmer profits. Their report, based on 147 studies, was published on November 3, 2014.

“Many people in Europe believe GM crops do more harm than good,” explains Qaim. “We felt that a publicly funded analysis of studies carried out worldwide would be a useful contribution to the public debate.” The results indicate that farmers employing insect-resistant or herbicide-tolerant GM seeds earned 6% higher profits and 21% higher yields, while using 37% fewer pesticides, as compared to farmers utilizing non-GM seeds. Hoping to quell fears about industry funding and publication bias, Qaim also incorporated data from studies not published in journals, such as working papers, conference presentations and reports in institutional series. Over 90% of the studies included were funded by public-sector sources. “A typical allegation is that a study showing benefits must have been funded by industry, so results may be influenced by private-sector interests,” says Qaim. “But the results don’t support that argument.”

Another widely cited concern is that journals would only publish studies with significant benefits. “We didn’t find any evidence of such publication bias,” he notes.

In addition, some GM-crop skeptics fear that the economic and agronomic benefits they provide are only short-term. “This is often mentioned in connection with resistance development in insect pests or weeds,” Qaim says. But resistance development is not an issue that is specific to GM crops. “This can also occur with conventional and biological pest control technologies, and it happens faster when good agricultural practices aren’t followed,” he says. The bottom line: farmers cannot substitute GM seeds for recommended agronomic techniques, such as crop rotation. As Qaim puts it, GM seeds “are not magic bullets.”

As European consumer polls call for more public information, Qaim continues to participate in the GM debate by addressing public concerns through his research. He notes that even in the face of clear scientific data, it may take some time to overcome public distrust, as has been the case with countless other scientific advances in history. Still, Qaim remains hopeful. “I’m optimistic that more evidence about the benefits of GM crops will contribute to wider public acceptance in the future.”

The Modi Operandi

Tackling India’s social problems with IT

By Zach Goldberg

In 2001, the Western Indian state of Gujarat—known locally as the “Jewel of the West”—was deep in the doldrums. Years of political instability, mismanagement and corruption had frayed away precious resources. The public cried out for a savior. Instead, they got an earthquake that killed 20,000 residents, destroyed nearly 400,000 homes and caused over US$5.5 billion in damages. From the fallout, Narendra Modi, a former tea peddler and science enthusiast, was catapulted into power.

Gujarat’s unpopular government intended for him to be the deputy chief minister. But Modi refused. “I’m either going to be fully responsible for Gujarat, or not at all,” some called him arrogant, if not authoritarian. In truth, Modi simply understood science and technology’s ability to solve the seemingly unsolvable. His model is simple: Lay the infrastructure—electricity, roads, schools, public transportation, broadband and so on—and harness information technology (IT) to streamline governance.
and achieve synergy between public officials and grassroots society. Such a model calls for far-flung flows of critical, often scientific, knowledge from one’s home. The “Modi model” worked wonders in Gujarat, now India’s premier e-governed state. Today, all 18,000 of its villages enjoy nationally unparalleled 24-hour electricity and Internet access, 95% of its electronically submitted public complaints have been addressed and its GDP and agricultural sector have grown at 10% and 9%, respectively, over the past decade. Having been elected, overwhelming, as India’s Prime Minister in May 2014, Modi is poised to work his magic at the national level. Challenges—including limited funds, infrastructural shortcomings and stifling regulatory environments—abound. Nonetheless, with hulking trains, “smart cities,” new solar projects and scientific research hubs in the pipeline, Modi has faith in the force multiplying effects of science and technology. Consider Modi’s “Digital India” campaign, by expanding broadband and mobile Internet coverage across the country, virtual medical technologies can then be used to ameliorate a health crisis compounded by the 700 million Indians who live isolated from the nearest hospitals. On this front Anita Goel, CEO of Nanobiosym and developer of the Gene-RADAR technology—a wireless iPad-sized diagnostic tool that rapidly tests for many diseases at a cost of just a few dollars—has been discussing plans with Modi “to place this mobile device in every village throughout the country.”

India faces an arduous road ahead, but the significance of Modi’s undertaking cannot be overstated. Modi, says Goel, “wants to turn India into a technological wellspring. But most of all, he wants to inspire hope in hearts around the globe.”

**NEUTRALIZING NEGLECT**

**Japanese experts collaborate locally and internationally to fight neglected diseases**

BY ICHIKO FUYUNO

Although Japan ranks third worldwide in developing new pharmaceutical products, its contribution to global health lags far behind. That imbalance may be shifting, however, with the launch of the Global Health Innovative Technology (GHIT) Fund, the world’s first public–private partnership dedicated to supporting global health R&D.

Since its establishment in 2013, the Tokyo-based, US$100 million initiative has funded 30 partnerships between Japanese and non-Japanese companies and public institutes aiming to develop drugs and vaccines to treat malaria, tuberculosis and neglected tropical diseases. These conditions affect over a billion people—most of them living in poor conditions in Africa—but limited financial returns prevent most major pharmaceutical companies from investing in research to treat them.

“The GHIT Fund addresses an important market failure,” says BT Slingsby, the fund’s CEO. “The demand is there, but the global society cannot be Undertaking but the road ahead, but the significance of Modi’s undertaking cannot be overstated.

**GREEN SKIES AHEAD**

**Norwegian wood may power tomorrow’s air travel**

BY NANCY BAZILCHUK

With more than 2,500 kilometers of coastline rumbled by deep fjords and rugged mountains, Norway seems tailor-made for the next decade for biofuel projects. A 2013 study commissioned by Avinor and the Norwegian airline industry concluded that Norway could sustainably produce up to 230 million liters of biofuel from wood products at competitive prices by 2025. “There is a need and space for aviation in the joke that ‘When God created Norway, he was thinking about aviation.’”

Now, a coalition of forest industries, environmental organizations and aviation companies hope to make air travel in Norway greener by laying the groundwork for aviation biofuels. In November 2014, two jets operated by Norway’s two major airlines, SAS and Norwegian, flew between domestic airports with a 48–52 blend of biofuel and conventional A-1 jet fuel. The blend cuts carbon dioxide emissions by 80% compared to regular jet fuel. In addition, Oslo Airport is the world’s first biofuel “hub,” where biofuel will be supplied through the fuel pipelines and hydrants.

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In spite of the costs, the Lufthansa Group, SAS and KLM have signed an agreement to purchase biofuel from the Oslo-Oslofjord area, Tachi Yamada, who previously received by Tachi Y amada, who previously led the Bill & Melinda Gates Foundation’s Global Health Program and is now chief medical and scientific officer at Takeda Pharmaceuticals, Japan’s biggest pharma company. Five pharmaceutical firms, including Takeda and Eisai, helped jumpstart the fund’s selection committee and advisory panel, which includes some of the world’s leading authorities on infectious disease.

Experts outside Japan also agree that GHIT is already having an impact. For instance, Medicines for Malaria Venture (MMV)—a nonprofit research organization in Switzerland—has formed 10 partnerships with Japanese pharmaceutical companies, including one with Takeda to test a new drug for malaria.

MMV’s CEO David Reddy says the fund is effectively helping Japanese pharmaceutical companies, which are “looking to globalize themselves, dedicated to social responsibility and hold a rich chemical library.” He adds, “We share the same sense of responsibility and strong willingness to work together.”

Slingsby, the fund’s CEO. “The demand is there, but the global society cannot be Undertaking but the road ahead, but the significance of Modi’s undertaking cannot be overstated.

**GREEN SKIES AHEAD**

**Norwegian wood may power tomorrow’s air travel**

BY NANCY BAZILCHUK

With more than 2,500 kilometers of coastline rumbled by deep fjords and rugged mountains, Norway seems tailor-made for the next decade for biofuel projects. A 2013 study commissioned by Avinor and the Norwegian airline industry concluded that Norway could sustainably produce up to 230 million liters of biofuel from wood products at competitive prices by 2025. “There is a need and space for aviation in the joke that ‘When God created Norway, he was thinking about aviation.’”

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Jing filgrastim, in March 2015. Approved its first biosimilar product, a
has approved 20 biosimilars, and the
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and the United States, opening the
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Park, Polpharma's biologic unit hopes
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EMA in the next few years, according to Klaudia Martin,
the company's head of biologics.
"Like generics, biosimilars are
very important to rein in health-
care spending and allow wider
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quite a cost-competitive set-up," he says. "If you look at originator drugs,
many of these use technologies that
were available 10, 15, 20 years ago.
The cell lines they used years ago
were nowhere near as productive as
modern systems." The first biologics manufacturing
facilities relied on large, dedicated
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pipes that required time-consuming
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tication bags. The single-use bags are
incinerated onsite, says Martin, and
even help generate electricity at the
Gdansk plant, further reducing costs.
Production can be scaled up quickly
by operating fermenters in parallel.
He adds that very few pharmaceutical
companies have bothered to re-engi-
nier their cell lines to achieve higher
productivity with existing biologic
drugs, because doing so would entail
new rounds of expensive clinical trials
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scholar in Russian studies at Harvard University. "They've got to come to the realization that a high-tech country possesses those ingredients in the society that make the development of high technology self-sustaining. It doesn't have to be ordered from above. If you get the right ingredients together, it will take off on its own."

Graham characterizes Russia's failure to achieve success commensurate with its intellectual firepower as, in part, an attitudinal problem that stems from its distain for business as a "disreputable activity." Even today, with the rise of Russia's middle class and an emerging business community, Russian scholars maintain negative attitudes about commercializing their inventions, he says. Graham does concede that there are calls for commercialization of technology among Russia's growing business class and in its schools of management. Still, he finds that the attitudes of many innovators remain mired in a distain for the "bourgeoisie."

Nonetheless, Graham sees some hopeful signs for Russia's economic future, such as systemic changes in the way it invests in science and technology. New institutions like the Russian Foundation for Basic Research (akin to the U.S. National Science Foundation) and such venture capital funds as Maxwill Biotech have been established, making it possible for individuals and small groups to seek funding outside of state control and direction. In addition, foreign technology companies have made inroads and forged collaborations with Russian scientists and nascent entrepreneurs. Yet foreigners with available cash don't feel legally secure investing in Russia, according to Graham. Reforming Russian laws to provide businesses with greater intellectual property protections, he says, would go a long way toward improving the country's economic prospects. Otherwise, Russia will continue to stagnate, as it could, or as Graham describes it, "its "consistent record, both brilliant and dismal."

"The ocean currents are very favorable to us, and there are industrial-scale quantities of seaweed!" The currents bring a large brown algae species that is of particular interest, Fowler says, called Laminaria hyperborea—8 to 10 million tons of it, with sustainable annual yields of 100,000 to 200,000 tons. This bounty of seaweed is not only used in its raw form as organic fertilizer and an animal feed supplement, but also provides a grilling agent called alginate, made up of "acids from its cell walls, which can be used in food processing. In fact, it was the Scottish chemist E.C.C. Stanford who discovered alginites in the 1880s. Fowler and Brown support increasing seaweed harvests through the development of sustainable and "extensive farms for biorefining of alginites and other high-value chemicals with byproducts for biofuels," Fowler says. Brown notes a "potential for a virtuous cycle" if these seaweed farms can be located near Scotland's sprawling fish farms—salmon alone is a $US2 billion industry—to "tie in with environmental remediation." That is, to sop up nitrogen from fish excrement. "There's a real synergy there," Fowler says, with "fish farm and seaweed side by side [and] with other species grazing on the seaweed that have a harvestable value as well—sea urchins, sea cucumbers.

Researchers at Scottish companies have been investigating seaweed and its microscopic cousin, microalgae, for a variety of uses. Fowler explains, including nutritional supplements, anti-aging creams and other "cosmeceuticals," or pharmaceutical-cosmetics hybrids. In addition, Scottish biotechnologists see other natural-product targets that fit today's greening philosophy. For example, the Scottish firm CelluComp converts vegetable processing waste from carrots and beetroot and other naturally derived waste into pigments, specialty celluloses, coatings and rheology products.

Not surprisingly, Fowler points out, deriving products from nature fosters collaboration between academia and industry. Research partners include the University of the Highlands and Islands' Scottish Association for Marine Science, the Industrial Biotechnology Innovation Centre and large companies like Unilever, Croda, DSM and BASF as well as more specialized ones, such as GlycoMar, which screens marine organisms for useful polysaccharide compounds and supplements.

Brown says the research-business crosspollination is beginning to pay off. At his first Natural Product Biotechnology meeting in 2009, 50 people showed up, mostly academicians. "We thought we were doing quite well," he says. But when the group met last fall, the gathering had swelled to more than 300 attendees, including 80 businesses—many of them casting an eye toward Scotland's seaweeds, its most abundant and undulating of natural resources.

BY BILL CANNON

SEA OF GREEN
Seaweed may be the solution for Scotland's natural-products industry

SYNONYMOUS WITH GOLF AND whiskey, Scotland brims with something else that might one day help define this nation: seaweed. At least that's the hope of biotechnology boosters Donald Fowler and Jim Brown.

Fowler, based in Argyll, is senior development manager for life sciences with the Highlands and Islands (HIE), a government economic and community development agency for the north and west of Scotland. Brown directs the annual Natural Product Biotechnology conference in Inverness. "There's a huge resource of kelp forest off the west coast," Brown says.

FROM RAPID TO LAB
Fighting infections the natural way

BY BILL CANNON

More spider than crustacean, the horseshoe crab resembles a ta- rantula wearing an old army helmet. It's a liv- ing fossil, its basic design unchanged for 440 million years. And the Atlantic horseshoe crab, Limulus polyphemus, can survive out of water for weeks, on beaches from Maine to the Yukon. Moreover, royal bluebloods have nothing on the horseshoe crab. Its blood really is blue, enlisting copper, rather than iron, to transport oxygen. That blue blood—says John Dubczak, general manager of the endotoxin and microbial detection division of Charles River Laboratories, a $US1 billion-plus global contract research organization with headquarters in Wilmington, Massachusetts—is remarkable at detecting harmful impurities in pharmaceuticals and medical devices.

Charles River has built its endo- toxin and microbial detection busi- ness by harnessing the crab's natural defense against infection: at the first sign of a toxin, the blood clots to block further spread. The company's Limulus amebocyte lysate (LAL) test detects this clotting reaction and is "the most sensitive in the world for bacterial endotoxins," says Dubczak, who is based in South Carolina, where he supervises the capture, blood collection and safe return of crabs to the sea.

Endotoxins or "pyrogens"—from the Greek for "fire" because they cause fever—reside in cell wall membranes of E. coli and other so-called gram- negative bacteria that can induce lethal bloodstream infections. These "dead bug parts," as Dubczak calls them, in a concentration of 79 parts per billion, "will make a person sick." Limulus blood clots when it encoun- ters an endotoxin concentration of just 1 part per trillion.

"You've seen an IV bag?" Dubczak asks. "The solution in that bag has to be tested for the absence of these pyrogens using our LAL reagent." So do the tubes and needles connecting the bag to the patient.

Until Charles River pioneered the test in the 1970s, labs tested for pyrogens by exposing rabbits to the substance in question and then checking them for fever. The LAL is much less cumbersome, much more sensitive and is now the standard worldwide. What's more, the horseshoe crab is a renew- able resource. Technicians can remove up to a quarter of the crab's blood without harming the animal, which is held for less than 24 hours. Dubczak meets annually with a state natural resources official, crab suppliers and handlers to discuss best practices for minimizing loss as crabs are shuttled between the ocean and lab and back. In the early 1990s, alarmed by dwindling crab populations, Charles River found itself in an unusual position for industry—lobbying for more regulation. South Carolina now limits times and places where crabs can be collected and bans their use as bait. Consequently, crab populations rebounded.

In recent years, Charles River invented a cartridge that requires 20 times less blood than its original assay. That's good for business and horseshoe crabs.
**WORLDVIEWPOINT**

**BY ROBERT HARIRI**

*AGING 2.0*

**Stem cells and digitized DNA may hold the key to high-performance longevity**

Although we can’t live forever, we can aspire to live much longer and healthier lives. In fact, living well into our 90s lies just ahead, if we keep fine-tuning the right tools. We start by understanding that aging arises from an accumulation of defects in our biology, and this causes joint decay, decreased muscle mass, Alzheimer’s and so forth. With digital health—basically, using high-performance computational tools to study complex biological processes—we can interrogate the cellular and molecular events that occur during human aging, and identify those that can be controlled or modified to slow or arrest those that degrade or degenerate our bodies over time. To make the most of digital biology, I joined forces with my friends and colleagues—Craig Venter and Peter Diamandis—to form Human Longevity, Inc. (HLI). At HLI, we combine knowledge from many areas of biology—the genome, proteome, biome and more—with advanced approaches to computing and informatics, all to create sophisticated cellular therapies. To build these treatments, we are collecting data from genomics and health outcomes from people around the world. All of that information will be combined to build powerful cellular therapies—actually developed from enhanced human cells—that will battle cancer, diabetes, obesity, heart disease, dementia and more. Further, these treatments will keep our bodies and minds performing as if they were younger and for a longer time.

Fundamentally, this work depends on making the most of tools that our bodies already possess, and I started thinking about these tools years ago.

**FROM TRASH TO TREATMENT**

Early in my medical career, I specialized in the repair of head and spinal cord injuries. With one patient, a defect in the tissue that surrounds the brain, the dura mater, needed to be repaired after a serious head injury. I realized, from my ob/gyn rotation, that the amnion—this amazing, clear plastic-like tissue that surrounds an embryo—seemed like the tissue around the brain that I needed to replace. That moment spawned other ideas about biological tissues being used in new ways. In particular, I started thinking that the placenta—the leftovers of birth—could be used as a source of stem cells. Instead of just throwing away the placenta after birth, we could make use of it. My personal “eureka moment” led me to form Anthrogenesis, which later became Celgene Cellular Therapeutics, where we mined the placenta as a source of pluripotent stem cells that can be turned into treatments.

A stem cell carries the remarkable capacity to participate in renovation or repair at any place in the body. Moreover, we can get these cells from many places beyond the placenta, including bone marrow and even fat tissue. Stem cells all “think” they are still in a fetus, and that is perhaps the most regenerative environment of all. In fetal surgery, for instance, you can open the uterus early in a pregnancy, perform surgery on the fetus, close up and let the baby come to term—and you won’t see a scar. You won’t see any evidence of the surgery at all. So a fetus can be more specialized at every step. We can watch such a change under a microscope, as this primordial cell turns into a heart cell or a neuron—all depending on its surrounding environmental cues that drive the DNA to create different things.

This DNA makes up a sort of biological software. Like lines of digital code, the genes in the DNA can be processed to drive an action, like generating a protein. As a stem cell develops into a specialist like a neuron, though, it loses the ability to be anything else. That neuron, for example, can’t turn on the genes that make a heart cell. And this is what happens as our cells age—they lose their versatility. At some point, we lose the ability to rejuvenate.

As we gather data on human genes and the outcomes that they create, healthcare experts can turn that knowledge into treatments for disease and to fight ordinary aging. In short, we must find ways to replenish the regenerative engine, and we do that by replenishing the reservoir of stem cells that provide synthetic versatility. With this knowledge, we can identify defective products—cells or tissues or organs—and then use stem cell-driven synthesis to restore the function of those parts. Doing this, though, depends on a deep understanding of how the biological software, a stem cell’s DNA, drives repair in its youth and loses that ability with age. So by better understanding aging and the molecular changes that drive it, we can learn to slow it down or work around it in places. We can find ways to use stem cells—maybe our own, those from someone else or from a placenta—to control certain diseases or to restore functionality as we age.

The future of stem cells and the future of cellular medicine will benefit from this analogy with computers and digital processing. Your software, your biological software, that is, resides in the nucleus. It’s not that different than having binary code that resides in the memory access of a computer. This thinking leads us to the concept of reprogramming the biological software of stem cells, which is already happening in activities to create induced pluripotent stem cells. These tools provide a platform for controlling fate and function, and they have broad biomedical applications. The most exciting one to me is prolonging and extending the quality of life.

Robert Hariri is the founder and chairman of Celgene Cellular Therapeutics, where he turns stem cells into therapies for many diseases; cofounder and vice chairman of Human Longevity, Inc.; and founder and chairman of Myos Corporation, a company developing products that improve the health of muscle. He trained as a neurosurgeon, is an avid jet and high-performance aviator and has produced several feature films and documentaries.

Opinions expressed in WorldViewPoint do not necessarily reflect those of the editors.
A WORLD FREE FROM CANCERS
Medical innovation makes life valuable and healthcare affordable

For more information about Celgene and its deep and diverse pipeline of innovative therapies, visit www.Celgene.com.