SCIENTIFIC AMERICAN

# worldVIEW

A GLOBAL BIOTECHNOLOGY PERSPECTIVE


THE POWER OF COMMUNICATION | DNA AS ANTI-AGING SOFTWARE | BEATING BLOOD CANCER

+ THE 7TH ANNUAL WORLDVIEW SCORECARD

PARTNER PROFILE

# Addressing the Barriers to Patient Access

**By STACEY L. WORTHY, Esq. / Director of Public Policy, The Alliance for the Adoption of Innovations In Medicine**

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.

***"We have a health insurance failure for innovative medicines. If you get cancer today, your copays can prevent you from accessing the medicines you desperately need. That's a failure of health insurance."*** Tomas Philipson, Ph.D., Professor, University of Chicago

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 their insurance companies finally agree to pay for the drug prescribed by their doctors.

One disturbing and wasteful insurance practice is what is euphemistically called "step therapy" or "fail first." In this practice, although a doctor may prescribe a medication most suitable to the patient's individual needs, the insurance company usurps the doctor's prescribing authority by requiring the patient to first fail on several inferior medications 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 legislatures to cap co-pays 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 time to end the adherence conundrum by reducing the cost-sharing barriers for cancer patients, so they can fill their prescriptions and take the medicines they desperately need.

It's the right thing to do for patients, the healthcare system and our economy.

## CONTACT YOUR ELECTED OFFICIAL to Support Patient Access to Medical Innovation

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**American Society of Hematology**
ORAL CANCER DRUG PARITY:
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SPECIALTY TIERS/CAP THE COPAY:
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**International Myeloma Foundation**
ORAL ANTICANCER TREATMENT ACCESS LEGISLATION:
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## RIGHT PATIENT, RIGHT MEDICINE, RIGHT NOW

**By JONATHAN WILCOX / Policy Director, Vital Options International**

**It may seem obvious to proclaim that the cancer patient journey is one of crossroads moments and good news/bad news scenarios. But perhaps now more than ever, the oncology world is stirred by astonishing breakthroughs in lifesaving medicines simultaneous with ever-higher and more complex barriers to access for patients who need them.**

**When it comes to the science of cancer, these are definitely the best of times. Exciting discoveries occurring in every area of cancer research are producing treatments targeted to the unique molecular and genetic characteristics of each person's cancer. Add the excitement over new immunotherapies that train a patient's immune system to destroy cancer and it is clear that the transformative change of precision medicine is well underway.**

**For some cancer patients seeking to utilize these life-saving therapies, however, all the world's medical innovation might as well never have occurred. Even as medical advances create new, potentially life-saving medicines for patients – and more quickly than ever before – ready access to these life-enhancing therapies is not assured.**

**Why? The path is blocked in two critical ways.**

**The first is governmental. What we call "new" cancer treatments are often 8-10 years old by the time they reach patients. Why isn't this a matter of months? The main reason is that FDA regulations were designed to evaluate the modernism of the VCR and 8-track tapes. Appropriate for their time, perhaps, but increasingly ill-equipped to co-exist with today's speedy scientific advances.**

**The second is access. Tens of thousands of cancer patients are customarily 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 surely does not want to be seen as standing in the way of sick people and their disease-altering treatments.**

**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.**

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# LET'S GIVE 'EM SOMETHING TO TALK ABOUT...

LETTER FROM THE EDITORS

The cornerstone of *Scientific American Worldview*—our annual Scorecard, evaluating the life science innovation capacities of countries around the globe (page 36)—emerged from a desire to bring a much-needed critical eye and third-party transparency to the international landscape of biotechnology. We are proud to have done this for seven years now, adding an objective, data-driven voice to an arena with a lot of unchecked cheerleading. This year, we add another data-led feature—albeit far less quantitative—titled *The Worldview 100* (page 8), celebrating the most influential people in biotechnology, as determined through nominations and selections from our international panel of experts. As with any list, this one will surely spawn differences of opinion about the people on it and those missing. Ultimately, though, driving discussion lies at the heart of this publication's mission. We want to encourage readers to explore biotechnology from a broad and global perspective.

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

Two sections—one on turning an idea into a product (page 22) and another on the successes, failures and future directions in communication about biotechnology (page 30)—trigger fresh ways of thinking about these topics. We continue this focus on fostering new dialogue with articles about the impact of location on drug development (page 66) and which countries excel and flounder when it comes to attracting biotechnology investment (page 68).

We did not, however, set out to spark debate from every element of the 2015 *Scientific American Worldview.* And few are likely to contest one "list" in this year's edition, which highlights some of the top innovators in medicine and two of the patients who reaped the benefits (page 72) of modern medical ingenuity. As in previous years, our "Country Spotlights" section (page 76) will take readers on a tour of science-in-action, showcasing biotechnology success stories around the planet.

Last but far from least, the worldVIEWpoint (page 84) essay reveals a modern, data-infused approach to finding a science-based "fountain of youth." The author, a pioneer in stem cell therapeutics, describes his journey into this field with an ironic story about turning what was once considered medical waste into cutting-edge medical treatments. His success proves that life-changing advances can and do materialize from highly surprising sources.

But that's just what we seek to uncover—the stories in which something unexpected makes the difference. One of the guiding themes of *Scientific American Worldview* is that innovation and ingenuity can occur in the most unlikely places. We've found evidence of that in every edition of our Scorecard. As our ranking system shows year after year, small or resource-challenged countries can dominate various aspects of biotechnology achievement, and even the giants can tumble on some metrics. This dynamic and developing industry continues to intrigue and amaze us. And we are once again delighted to bring you the people, places and perspectives that are moving it forward.

As always, we offer our profound thanks to our sponsors and partners: Celgene Corporation, Cure Forward, Credible Meds, and The Biotechnology Industry Organization.

Sincerely,

**Jeremy Abbate, Publishing Director**
**Mike May, Editorial Director**
**Yali Friedman, Head, Data Analytics**






## PUSHING P4

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 medical practice and reimbursement—randomized clinical trials (RCT) and comparative effectiveness research—are dangerously broken.

There is a broad bipartisan effort to move towards personalized and precision medicine because getting the right treatments to the right patients at the right time can reduce the cost of healthcare and save lives. But good policy has to be guided by good science and a systems-driven medicine that is predictive, preventive, personalized and participatory (P4). Marginal changes to evidence-based medicine (e.g., computerizing data collection) will themselves have only marginal effects on improving healthcare and reducing its costs. Specifically, the RCT, our gold standard, typically fails when there is multicausality for any disease, phenotype or biological feature(s) of clinical importance. Medicine is empirically, and with some knowledge of mechanisms, climbing multi-peaked clinical landscapes successfully—where RCT fails. In addition, patients are unique genetically and environmentally, and hence should not be averaged in large populations. Rather, the personalized multidimensional data clouds of each individual should be analyzed independently, and then patients with similar features can be aggregated into related groups of interest (e.g., those responding effectively to a drug). We are throwing away unknown hoards of relevant data about both the variability of response and multiplicity of causes at the genetic and phenotypic level when we average patient populations. With the analysis of individual patients we can gain fundamental new insights into disease through N=1 experiments and appropriate statistical power can be gained through the aggregation of related patients.

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

Further, the one drug–one disease model of innovation (based on Pasteur's germ theory) is outdated. Genetic, environmental, behavioral and demographic factors regulating well-being have turned single illnesses, such as cancer, into multidimensional diseases for which no single drug can be successful. Cells, tissues, organs and organ systems are networks of causal interactions, best treated by smart combinations of drugs, nutriments and other strategies, such as immune therapy. Yet, virtually every researcher, company and regulatory agency is organized around the one drug–one disease business model.

Consumers—via social networks, multi-dimensional data clouds and digital tools—are deciphering biological complexity to match people to combinations of treatment. They are bypassing large clinical trial networks to get better answers more quickly with individualized approaches to their disease. We should enable this movement to accelerate personalized medicine.

COLIN HILL
LEROY HOOD
SUI HUANG
STUART KAUFFMAN
—founders of Transforming Medicine: The Elizabeth Kauffman Institute

## TRANSFORMING THE FUTURE OF HEALTHCARE

In the past two decades, the pace of medical progress has accelerated. The human genome has been sequenced, hepatitis C can be cured, HIV has been turned into a chronic condition and remission has become more common and attainable in several forms of cancer.

Despite progress, challenges remain in translating basic science discoveries into medical practice. Whereas the 20th century saw a focus on developing better treatments for disease, there has been far less attention to prevention, early detection and interception of disease.

The impact of conditions like Alzheimer's disease, cancer, rheumatoid arthritis and diabetes continues to burden global healthcare systems. Patients affected by these diseases often spend years of their lives in a state of declining health. According to the U.S. Centers for Disease Control and Prevention, in the United States alone, about half of all adults, 117 million people, live with at least one chronic condition.

Earlier this year, Janssen Research & Development, one of the Janssen Pharmaceutical Companies of Johnson & Johnson, announced the launch of three new research platforms focused on disease prevention, disease interception and the mi-

crobiome. These new teams will collaborate closely with Janssen's five therapeutic areas and external partners to propel science in an effort to change an approach from "disease care" to health care.

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 taking advantage of our ability to rapidly sequence the human genome, we are able to understand an individual's susceptibility to disease, calculate one's risk and intervene before illness occurs.

Today, early disease interception and prevention strategies are still largely unexplored for many of the illnesses that plague our societies. The Janssen Prevention Center (JPC) will focus on the prevention of chronic, non-communicable diseases such as Alzheimer's, heart disease, cancer and autoimmune diseases, which increasingly impact aging populations and burden healthcare systems globally. The JPC will leverage the world-class vaccine discovery expertise of the former Crucell Vaccine Institute (The Netherlands) in collaboration with laboratories in the United States and United Kingdom to discover solutions to extend people's healthy life span.

The Disease Interception 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). Janssen scientists will work to develop new diagnostic, therapeutic or combination approaches for T1D interception by understanding the role of potential triggers and initiating steps on the pathway to T1D.

The Janssen Human Microbiome Institute (JHMI) was designed to explore the relationship of the organisms that inhabit our body in maintaining health and causing disease. Ultimately, this unique Janssen initiative will develop new ways to maintain health and treat disease. External collaborations for this organization will be fostered through anchor research centers located in Cambridge, Massachusetts, and Beerse, Belgium.

During the last 120 years, Johnson & Johnson has pushed forward many "firsts"—evolving from 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.

WILLIAM N. HAIT
Global Head
Janssen Research & Development, LLC
Raritan, New Jersey

## THE EBOLA-VACCINE FUNDING GAP

With the number of new cases of Ebola appearing to level off, and with clinical trials for Ebola vaccines now underway, there is an almost palpable sense that the crisis is over. The reality, however, is that even if a safe and effective vaccine emerges and the epidemic is brought under control, we are still in many ways no better prepared for future outbreaks than we were a year ago.

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 if, or when, a vaccine becomes available. Millions of doses will be needed, and not just to help end the current epidemic but also, crucially, as a stockpile to prevent future outbreaks from getting out of control.

The problem is that there is no market. It's one thing developing and approving a vaccine, and quite another getting it out to the people who need it the most. With a disease like Ebola, which kills ferociously but occurs sporadically and usually in remote areas, there simply is no commercial market. Who would buy it? Outbreaks usually involve only a couple of hundred cases and typically occur every few years in poor rural communities in Africa. So, manufacturers would be unlikely to see a return on that investment.

This means that even if one of these candidate Ebola vaccines receives clinical approval, we'll still be left with a significant funding gap. Gavi, the Vaccine Alliance, is committed to purchasing necessary vaccines for this outbreak and creating a stockpile for future outbreaks as well as incentivizing next-generation vaccine development, but as a public-privately funded global health organization we still have not yet determined who will provide these funds.

We need to stop waiting for evidence of a disease becoming a global threat before we treat it like one. If we want to prevent major outbreaks of diseases like Ebola then we need to invest in vaccine stockpiles and start viewing them as the ultimate deterrent—making sure they are there, and at the same time praying 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$215 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. These personalized stem cells provide a more comprehensive system for understanding the behavior of particular diseases than current genetic sequencing approaches available. These cells enable us to study diseases—Parkinson's and Alzheimer's, ALS, muscular dystrophies, epilepsy, diabetes, cardiomyopathies and macular degeneration, among others—at the phenotypic level (i.e., how the cell's behavior or function is affected) rather than just via genotype.

iPSC technology also offers the potential for a unique approach to precision medicine: personalized cell transplants. A first look at this potential may come from the National Eye Institute and its collaboration with Cellular Dynamics International (CDI) that ultimately may lead to a treatment for macular degeneration with an autologous (the patient's own) iPSC-derived retinal cell transplant. This is expected to lead to the first clinical trial in the United States using iPSCs.

The convenient criticism of personalized medicine is the perceived cost. But the price should decline, just as the cost of sequencing the human genome rapidly declined. The time is right for the United States to fully embrace this rapidly developing field with research dollars. Personalized medicine has arrived, and the United States needs to lead this race to the finish line.

BOB PALAY
CEO and Chairman
Cellular Dynamics International (CDI)
Madison, Wisconsin

**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.**

## 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 this unmet medical need with the Beat AML initiative.

Beat AML needs to also consider the impact clinical trial management has on commercial success and the nuances surrounding proper hematological oncology study design. Because hematologic oncology trials are fundamentally different than a solid-tumor study, it can be quite challenging to develop and implement successful trials. Oncologists and drug developers need to understand that by better addressing the treatment agendas of individual patients, the more success the study will have in recruitment and completion.

Unlike tumor-based cancers, which are classified based on their point of origin in the body, hematological malignancies, such as AML, can develop into new cancers as they progress, making them very hard to define. The specificity of the disease also makes developing targeted therapies especially critical to treating them. Advancing research through genetic testing and affecting change in the regulatory process should remain key areas of the initiative's multi-pronged approach. However, clinical trial management can't be forgotten.

Enhancing and refining our understanding of these cancer pathologies can increase the number of targeted therapies to enable truly personalized treatments. Moreover, ensuring careful trial design and precise trial execution will yield data that can inform, and perhaps significantly impact, the greater oncology community.

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# 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 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 constructively 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.**

### THE WORLDVIEW 100 SURVEY METHODS

*We developed and finalized this list in several steps through a process carried out from December 2014 through March 2015. First, we invited dozens of leaders in biotechnology and biosciences to nominate their choices for the most influential people in the field. We encouraged the nominators to select living experts currently working in the sector from a range of contributing areas, including industry, academia, public policy, finance, law and beyond. That process generated a list of almost 400 nominees. We then recruited more experts—many of them from the original group of nominators—to suggest anyone on the list of nominees worthy of selection to a more refined coterie of the 100 most influential figures in today's world of biotechnology. For the final step, we tallied the votes, and the 100 people most selected formed The Worldview 100. Here, we highlight the 10 individuals who received the highest number of votes. We present the other 90 honorees in alphabetical order.*

# YOUR TOP 10

## GEORGE CHURCH

**professor of genetics | Harvard Medical School | Boston, Massachusetts, U.S.**

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 *Regenesis*, coauthored with science writer Ed Regis, "a valuable glimpse of science at the edge."

## FRANCIS COLLINS

**director | U.S. National Institutes of Health | Bethesda, Maryland, U.S.**

"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."

## BILL GATES

**co-chair and trustee | Bill & Melinda Gates Foundation | Seattle, Washington, U.S.**

Best known as the cofounder of Microsoft, Gates turned his wealth into philanthropic giving through his and his wife's foundation, which, its website states, works to "bring about the kinds of changes that will help people live healthier and more productive lives." Clearly, innovation has always played a fundamental role in his career. He once noted, "I believe in innovation and that the way you get innovation is you fund research and you learn the basic facts." That thinking took him a long way.

## MELINDA GATES

**co-chair and trustee | Bill & Melinda Gates Foundation | Seattle, Washington, U.S.**

In her 1982 high school valedictorian address at Ursuline Academy in Dallas, Texas, Melinda Gates offered the following wisdom: "If you are successful, it is because somewhere, sometime, someone gave you a life or an idea that started you in the right direction. Remember also that you are indebted to life until you help some less fortunate person, just as you were helped." At that time, no one could even imagine the help that she would bring to the world. According to her foundation's website, it has given grants totaling US$32.9 billion.

## PEGGY HAMBURG

**former commissioner | U.S. Food & Drug Administration | Silver Spring, Maryland, U.S.**

Born to a two-physician family, Hamburg joined the family business—but in a managerial capacity. Before working for the FDA, she served as commissioner of the New York City Department of Health and Mental Hygiene, where she significantly slowed the spread of tuberculosis. When President Obama named Hamburg the FDA commissioner in 2009, Georges Benjamin, then executive director of the American Public Health Association, said, "She's all about integrity and science…. She can be tough when she needs to be, and she's going to need to be real tough in that job." How right he was.

## LEE HOOD

**president & cofounder | Institute for Systems Biology | Seattle, Washington, US**

Hood played a role in the development of five instruments that drive today's biological sciences: automated DNA sequencers, DNA synthesizers, protein sequencers, peptide synthesizers and an ink-jet printer for constructing DNA arrays. Today, he works on integrating biology, computation and technology to build so-called P4 medicine, which is predictive, personalized, preventative and participatory. In the 2012 *Scientific American Worldview*, Hood posited that the traits of a successful entrepreneur are "having a clear picture of the future that is very different from what other people have, and an ability to drive towards that future."

## ERIC LANDER

**professor of biology | MIT | Cambridge, Massachusetts, U.S.**

After publishing a 2005 article in *Nature* on the chimpanzee genome, Lander said, "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." As a core member of the Broad Institute, Lander continues to explore what genomics can tell us about human physiology and diseases—especially how to treat them.

## BOB LANGER

**David H. Koch Institute Professor | MIT | Cambridge, Massachusetts, U.S.**

Langer described his greatest contribution to biotechnology as "discovering how to create materials that enable the controlled release of macromolecules." Such devices can deliver drugs—even genetically engineered proteins—for long periods, and Langer is even working on versions that can be controlled through magnetic, ultrasonic and enzymatic methods. The best way to increase the effectiveness of biotech today, he said, is to provide "more funding for basic research." Langer's output—including more than 1,000 patents, which have been licensed to over 300 companies—attests to his indefatigable drive.

## CRAIG VENTER

**founder | J. Craig Venter Institute | La Jolla, California, U.S.**

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.

## JANET WOODCOCK

**director | Center for Drug Evaluation & Research | U.S. Food & Drug Administration Silver Spring, Maryland, U.S.**

Woodcock helped to develop a regulatory framework to accommodate future advances in biotechnology. Nonetheless, the discipline's effectiveness could be enhanced even more, she said, through "greater attention to translational science." So far, the biggest impact biotech has had on our daily lives is "the food revolution," she said, adding that "forms of gene therapy may be 'coming of age.'" And the most embarrassing moments of her career? "Too numerous to count!" she answered.

### NAGLAA ABDALLAH
**head | Agricultural Genetic Engineering Research Institute**
**Cairo University | Giza, Egypt**

Abdallah participates in the science and use of genetically modified crops in a variety of ways. 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**
**Infinity Pharmaceuticals**
**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 YMCA.

### MAHALETCHUMY ARUJANAN
**executive director | Malaysian Biotechnology Information Centre (MABIC) | Selangor Darul Ehsan, 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."

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

"Currently, there are not enough organs to go around," Atala declared at TED2011. He aims 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 BALTIMORE
**Robert Andrews Millikan Professor of Biology | California Institute of Biology**
**Pasadena, California, U.S.**

In his Nobel Lecture, Baltimore said, "The study of biology is partly an exercise in natural esthetics. 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
**president & 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."

### SOL BARER
**managing partner | SJ Barer Consulting**
**Summit, New Jersey, U.S.**

"We are optimistic now that many fatal diseases can indeed not only be treated but potentially cured," said Barer, former CEO and chairman at Celgene. 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."

### ROGER BEACHY
**director | World Food Center | University of California, Davis | Davis, California, U.S.**

This plant biologist visionary and founding president of the Danforth Center knows how to keep things in perspective. "After a series of laboratory successes that followed the discovery of disease-resistant technologies, I self-assuredly referenced 'being on a roll,'" he told *Worldview*. "Soon thereafter I took a fall and a long roll down a run at the Purgatory ski resort at a Keystone Conference. To my chagrin and embarrassment, a friend, Jonathan Jones, from the John Innes Center, UK, shouted, 'Are you still on a roll, Beachy?'—not just one time, but repeatedly in following years."

### SETH BERKLEY
**CEO | Gavi, the Vaccine Alliance**
**Geneva, Switzerland**

On extending the global reach of today's cutting-edge medicines, Berkley opined, "Even stronger public-private partnerships will ensure that the products of this revolution are made available to those living in the poorest parts of the world. In my current job at Gavi, the Vaccine Alliance, we have used this kind of model to help developing countries deliver vaccines to more than a half billion additional children and prevented more than 7 million future deaths in the 73 poorest countries in the world."

### KAREN BERNSTEIN
**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 asserts. "There is no simple fix for this, but I think we must try."

### SANGEETA BHATIA
**director | Laboratory for Multiscale Regenerative Technologies | MIT**
**Cambridge, Massachusetts, U.S.**

"We're engineers working in a science environment, thinking about human health," Bhatia told NBC News. "What engineers like to do is tinker, so we encourage that spirit of tinkering in the lab."

### JACK BOBO
**senior advisor for biotechnology**
**United States Department of State**
**Washington, DC, U.S.**

"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."

### 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."

### DAVID BOTSTEIN
**CSO | Calico | South San Francisco, California, U.S.**

With genomes available for a growing list of organisms, Botstein takes the next step—using them to explore complete biological systems. This includes learning to analyze and display biology's genomic big data.

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

Regarding a new manufacturing plant in Singapore, Bradway recently told the *Pacific Coast Business Times*, "This is an approach to manufacturing that we think will enable us to reduce our cost per gram of proteins by an order of magnitude of about 60%."

> "This aversion to change has delayed the adoption of agricultural biotechnology in some parts of the world." —JACK BOBO

### STEVEN BURRILL
**CEO | Burrill LLC | San Francisco Bay Area, California, U.S.**

Looking back on biotech's history, Burrill opined, "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 in history as mankind's greatest moment—when we truly, for the first time, understood the basis of life and our ability to improve it, transforming healthcare, 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
**founding 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.

### ART CAPLAN
**Drs. William F. and Virginia Connolly Mitty Professor of Bioethics | New York University | New York, New York, U.S.**

As his biggest contribution to biotechnology, Caplan cited: "Helping to lay out the ethical case for moving advances forward while protecting human subjects." His most embarrassing moment? "Applying for a grant with Dan Callahan while at the Hastings Center in 1985 to study 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."

### ISAAC CIECHANOVER
**president & CEO | Atara Biotherapeutics South San Francisco, California, U.S.**

Over his 20-year career, Ciechanover has spurred numerous medical advances and driven mergers and licensing worth US$6.7 billion. He also cycles, scuba dives and loves Pink Floyd's *The Dark Side of the Moon*.

### RON COHEN
**founder, president & CEO | Acorda 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.

### STANLEY CROOKE
**CEO | Isis Pharmaceuticals Carlsbad, California, U.S.**

A pioneer who helped lead the creation of RNA-targeted drug discovery, Crooke told *Worldview* that the "one and only time I guaranteed a new drug would work in the next clinical trial was to the SmithKline Beckman board when I was president of R&D there. We had a vasopressin antagonist and it worked beautifully to increase free water clearance in all animal models. In man, it was a partial agonist and actually caused water retention."

### 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."

### PETER DIAMANDIS
**founder & chairman | XPRIZE Foundation cofounder, Human Longevity, Inc. Culver City, California, U.S.**

In a 2012 interview with *Wired*, Diamandis declared, "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." No wonder he created the XPRIZE, with its mission of "designing and launching large incentive prizes to drive radical breakthroughs for the benefit of humanity." Diamandis is also cofounder of Human Longevity, Inc., along with Craig Venter and Robert Hariri.

### JENNIFER 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 between academic labs and companies" to help biotechnology move ahead even faster.

### NINA DUDNIK
**founder & CEO | Seeding Labs | Boston, Massachusetts, U.S.**

"My goal, through Seeding Labs, is to ensure that as many scientists as possible have the right tools, training and professional networks to make impactful contributions to biotechnology," says Dudnik. "There is remarkable talent around the world, and developing capacity and infrastructure for these individuals is a smart, measurable investment in global science." She added, "Our responsibility does not end in the lab, especially in the digital age. We need to be ambassadors and translators for science."

### DREW ENDY
**associate professor Bioengineering | Stanford University Stanford, California, U.S.**

Endy, a synthetic biologist, told *The Guardian*, "I want to be able to design and build biological systems to perform particular applications. The scope of material I can work with is not limited to the set of things that we inherit from nature."

### OMID FAROKHZAD
**associate professor | Harvard Medical School | Boston, Massachusetts, U.S.**

An expert in developing nanoparticle-based systems of drug delivery, Farokhzad said of one of his recent studies: "This is the first example of a targeted nanoparticle technology that reduces atherosclerosis in an animal model." His work also explores nanomedicine's potential to treat many other diseases.

### NINA FEDOROFF
**Evan Pugh Professor of Biology The Huck Institutes of the Life Sciences Pennsylvania State University State College, Pennsylvania, U.S.**

Fedoroff pioneered the development of molecular cloning and analysis techniques for plants starting in the late 1970s, and today she would like to see governments "simplify their regulation and make the regulations product- and not process-based."

### JAY FLATLEY
**CEO | Illumina | San Diego, California, U.S.**

Flatley told *Worldview* that we are "moving into an era of greater diagnostic precision and personalization of patient care," such as non-invasive prenatal testing for chromosomal abnormalities and liquid biopsies to detect DNA circulating in the blood from cancer cells. He added, "I think one of the most meaningful impacts will be allowing us to live healthier lives longer."

### 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.

### ROBB FRALEY
**executive vice president and CTO Monsanto | St. Louis, Missouri, U.S.**

"The ability to identify and map every single gene in a plant, as well as create, screen and identify genetic combinations," he said, "has literally changed how we breed crops. Today, we are seeing record rates of gains and yields in crops where these advanced breeding techniques have been applied and as technology costs have rapidly declined, their impact is now reaching native and orphan smallholder crops."

### YALI FRIEDMAN
**Head, Data Analytics, Scientific American Custom Media | Washington, DC, U.S.**

"Fresh out of graduate school I published *Building Biotechnology*, which quickly became the leading textbook on the business of biotechnology," said Friedman. "Lately I have been developing a novel methodology to rank patent attorneys at PatentStat.com, building a tech transfer search engine at TechTransferWatch.com, and leading data analytics for Scientific American Custom Media."

### ANITA GOEL
**chairman & scientific director | Nanobiosym Cambridge, Massachusetts, U.S.**

Goel received the 2013 XPRIZE in recognition of her pioneering contributions to the new field of nanobiophysics and her Gene-RADAR technology, which she described in the 2014 edition of *Worldview* as "a mobile diagnostic platform for providing anyone, anytime, anywhere with instant access to personalized information about their health."

### HUGH GRANT
**CEO | Monsanto | St. Louis, Missouri, U.S.**

In discussing exciting advances in biotechnology, Grant said, "From new areas of research in agricultural biologicals to the intersection of data science and precision agriculture, the seamless use of a variety of technologies—including biotechnology—will transform the future of agriculture."

### JIM GREENWOOD
**president & CEO | The Biotechnology Industry Organization (BIO) Washington, DC, U.S.**

"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, then as a caseworker with abused and neglected children." Later, he was elected to the Pennsylvania State House, the Pennsylvania State Senate and the U.S. Congress. "When I was offered my position at BIO, I saw it as an opportunity to continue that focus on service," he explained.

### ROBERT HARIRI
**chairman & founder | Celgene Cellular Therapeutics; cofounder, Human Longevity, Inc. | Warren, New Jersey/ La Jolla, California, U.S.**

According to Hariri, "Biotech has been the source of virtually every major new platform of technology which creates new therapeutics, such as biologics, immunotherapy and cellular medicine. I believe cellular immunotherapy will have a quantum effect on the treatment of cancer in the next 3 to 5 years."

### DEBBIE HART
**president & CEO | BioNJ Trenton, New Jersey, U.S.**

"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 undying 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 HASELTINE
**chairman & president | ACCESS Health International | New York, New York, U.S.**

If Haseltine could make one change in the world of biotech, he would "create 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."

### LUIS HERRERA-ESTRELLA
**chief | National Laboratory of Genomics for Biodiversity | National Polytechnic Institute | Irapuato, Mexico**

If he hadn't gone into biotechnology, Herrera-Estrella told us, he might have been a professional dancer. Instead, he works on genetically modified (GM) crops, of which he said, "due to lack of information and the opposition of anti-technology groups, their full potential still has not been achieved. GM crops reduce the cost of production and the negative environmental impact of agriculture by reducing the use of agrochemicals."

### JAMIE HEYWOOD
**chairman & cofounder | PatientsLikeMe Cambridge, Massachusetts, U.S.**

When asked about the biggest impact of biotech on our lives, Heywood said, "What we have seen so far is like looking at the first computers and anticipating the iPhone and the Internet. Biotechnology is an information frontier that is just beginning to open and it will transform everything about how well and how long we live."

### BOB HUGIN
**chairman & CEO | Celgene Summit, New Jersey, U.S.**

"In the last 50 years, 50% of the economic growth in America is due to medical innovation…and 73% of life expectancy gain in the first decade of this century is due to medical innovation," Hugin recently told CNBC. "Intellectual property is the lifeblood of innovation, and we have to make sure as a company, as an industry, we protect it."

### CLIVE JAMES
**founder & emeritus chair | International Service for the Acquisition of Agri-Biotech Applications (ISAAA) | Cayman Islands**

"The contribution of biotech/GM crops to the alleviation of poverty and hunger," said James, is the most impactful effect biotechnology has had on our lives to date. "The commercialization by Bangladesh, one of the poorest countries in the world, of Bt brinjal (eggplant) can benefit up to 150,000 small resource-poor farmers."

### CALESTOUS JUMA
**director | Science, Technology, Globalization Project | Belfar Center for Science and International Affairs | Harvard Kennedy School | Cambridge, Massachusetts, U.S.**

Although Juma has more than 68,000 followers on Twitter, you don't need to follow his tweets long to understand his perspective. On March 21, for example, he tweeted a photo of a lion and zebra drinking side by side with the hashtag #peace.

### CARL JUNE
**Richard W. Vague Professor in Immunotherapy | Perelman School of Medicine | University of Pennsylvania Philadelphia, Pennsylvania, U.S.**

When we asked June what could drive innovative science that will benefit the healthcare system, he replied, "I think now we're at this real tipping point where we can harvest many of the basic advances, and things previously thought impossible will be happening. I think one thing is we need to educate the public about what can happen because the public will be more involved" with the new therapies.

### MARY-CLAIRE KING
**American Cancer Society Research Professor departments of medicine & genome sciences | University of Washington Seattle, Washington, U.S.**

King applies next-generation sequencing to a wide range of crucial areas, including breast and ovarian cancer, as well as the genetics of schizophrenia. In addition, she even uses sequencing to identify victims of human rights abuse.

### RACHEL KING
**president & CEO | GlycoMimetics Gaithersburg, Maryland, U.S.**

In her testimony to the U.S. Senate Committee on Small Business and Entrepreneurship on March 19, 2015, King eloquently distilled the relationship between science and business: "Patents allow biotech inventions of great societal value to be passed or shared among parties best suited to unlock their potential at any given stage of development and commercialization—each contributing its part, each sharing the risk of failure, each increasing the odds that a product eventually reaches patients."

### GANESH KISHORE
**CEO | Malaysian Life Sciences Capital Fund | St. Louis, Missouri, U.S.**

"The greatest concern I have," Kishore told *Worldview*, "is that the emotional and geographic barriers for the adoption of products of biotechnology have become globally rampant. In fact, it is troubling that our society fails to recognize that all food in our plant and even animal food chain today is 'genetically modified'—and even evolution is about genetic modification leading to adaptation."

"I would improve the communication of biotechnology's enormous value proposition to society." —JOHN MARAGANORE

### RAJU KUCHERLAPATI
**Paul C. Cabot Professor | department of genetics | Harvard Medical School Boston, Massachusetts, U.S.**

Kucherlapati told PhRMAdigital, "Personalized medicine has the potential to significantly alter the health and well-being of all of the American population. And if our population begins to recognize what personalized medicine is, how the principles of personalized medicine would apply to their health and well-being, it would have a very significant impact."

### ANNA LAVELLE
**CEO | AusBiotech | South Yarra, Australia**

In *BioSpectrum*, Lavelle recently wrote: "High-tech innovative industries generate globally competitive economies and sustainable, high-skilled jobs and Australian biotechnology is poised to make its contribution to Australia's growth. Australia has a strong comparative advantage in medical research and the calibre of its researchers, and in its ability to specialize in niche manufacturing."

### MARK LEVIN
**partner | Third Rock Ventures Boston, Massachusetts, U.S.**

Upon receiving the 2014 Leadership in Personalized Medicine Award, Levin remarked, "The best part of the last 40 years has been working with incredible people…to make a difference for patients. It cannot get any better than that!"

### ART LEVINSON
**founder & CEO | Calico South San Francisco, California, U.S.**

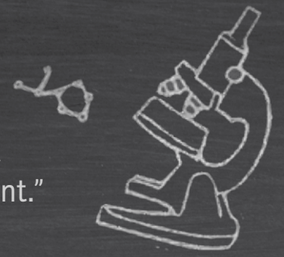
"As a little kid," Levinson once said, "I was always afraid of getting old. On my 7th birthday, I was actually sad, because it just seemed like—wow, 7 is not 6 anymore." No wonder he recently founded Calico, which plans to "devise interventions that enable people to lead longer and healthier lives."

### JOHN MARAGANORE
**CEO | Alnylam Pharmaceuticals Cambridge, Massachusetts, U.S.**

"While there's still more to do," Maraganore said, his chief contribution to biotechnology is "delivering on the promise of RNAi as a new class of innovative medicines." Regarding ways to make biotech more effective, he said, "I would improve the communication of biotechnology's enormous value proposition to society."

### ANDY MARSHALL
**chief editor | *Nature Biotechnology* New York, New York, U.S.**

Marshall described his greatest contribution to his field as "finding the best and brightest to work with me. And helping the best and the brightest junior faculty meet the best and the brightest in the business world. Not enough is being done to give gifted researchers the funding and opportunities they need. A lot of good science is falling between the cracks."



"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**
**Biocon | Bangalore, India**

In the 2011 edition of *Scientific American Worldview*, Mazumdar told us: "My philosophy has been one of differentiation. Look at what's there and keep challenging yourself to be different: If everyone is after generic products, how can you get into novel programs? If you can do that, then you stand apart and you can do things more effectively."

### 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 FDA 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."

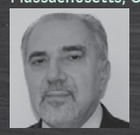
### DAVID MOTT
**general partner | New Enterprise Associates**
**Timonium, Maryland, U.S.**

After executive roles in pharma, Mott moved to healthcare venture investing in 2008, where he quickly made a name for himself. In fact, *FierceBiotech* called him the "leading life sciences venture maven," 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 she said, "launched and invigorated 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."

### STELIOS PAPADOPOULOS
**chairman | Biogen Idec | Cambridge, Massachusetts, U.S.**



In 1979, Papadopoulos started collecting biotech IPO data, and he recently showed that 2014 brought the industry 22% more IPOs than in 2000, the so-called bubble year. In the age of computation and big data, he still gets results the old-fashion way—he collects it by hand.

### 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 of Immunologists in 2013, "focus on grievous illness… focus on the task, not the tool…[and] do the experiment in people."

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

"The core 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 2012, 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."

### 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 anachronistic and propagate individual investigator-centric silos of reductionist biology, which lack critical mass and are ill-suited to address the complexity of unresolved disease challenges that require large scale, multi-disciplinary, team-based approaches, often involving multiple institutions."

He also won the prize for the best 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 resentful, the nadir was reached in my attempt to anesthetize a large tree porcupine from the local zoo by applying the anesthetic mask to the wrong end of what was a large, wriggling ball of spines, which prevented any easy effort to distinguish anterior and posterior axes."

### PAM RONALD
**director | Laboratory for Crop Genetics Innovation & Scientific Literacy | University of California, Davis | Davis, California, U.S.**

When *Worldview* asked Ronald to tell us her greatest contribution to biotechnology, she pointed out her work with rice, in particular, "isolation of the *Xa21* resistance gene and the *Sub1* submergence tolerance gene in collaboration with my colleagues." Her pick for the most exciting application of biotech in the past year: the HIV and Ebola vaccines.

### RAM SASISEKHARAN
**Alfred H. Caspary 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 glycobiology 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."

### GEORGE SCANGOS
**CEO | Biogen Idec**
**Cambridge, Massachusetts, U.S.**

"We're in a very exciting time in the biotechnology industry," Scangos 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."

### LEONARD SCHLEIFER
**founder, president & CEO | Regeneron**
**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 first time she took a deposition: "I got there early, and I thought that the most important thing was to control the witness. I didn't realize…the way you control somebody is not by intimidating them. But I adjusted the chair…so that I'd be really tall, and could look down imposingly on the witness. But I raised it so high that as soon as I sat down, I toppled over and fell backward."

### RAJIV SHAH
**distinguished fellow | School of Foreign Service | Georgetown University**
**Washington, DC, 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 #globaldev, especially in infrastructure. Be bold & creative going forward."

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

"My greatest contribution to biotechnology is novel science and translation of this science to helping people through cofounding and participating on the boards of Biogen Idec (1978) and Alnylam (2002)," Sharp said. "This has benefited millions of people around the world as patients and as well in the creation of new jobs."

### PATRICK SOON-SHIONG

**chairman | Chan Soon-Shiong Family Foundation | Culver City, California, U.S.**

"Soon-Shiong is rolling out a series of companies that represent a $1 billion-plus effort to fight cancer in new ways," *Forbes* recently reported. "This includes buying DNA sequencers to unravel the DNA of cancer patients, not in a clinical trial but as standard practice, at an unprecedented scale."

### PAUL STOFFELS

**CSO | Johnson & Johnson**
**New Brunswick, New Jersey, U.S.**

"The mission of our innovation centers is to find the best science available in an early stage, and then to accelerate it in order to stimulate the development of new healthcare solutions," Stoffels explains on a Janssen website. "By doing so, we have tracked down more than 2,700 valuable opportunities in 18 months and concluded some 80 collaboration agreements."

### JACK SZOSTAK

**Alex A. Rich Distinguished Investigator department of molecular biology**
**Massachusetts General Hospital**
**Boston, Massachusetts, U.S.**

"Is it easy or hard for life to emerge from the chemistry of early planets?" Szostak asked in an iBiology lecture. "Unfortunately, it's going to be a long time before we can answer that question in the most satisfying way, by direct observation." In his lab, though, Szostak seeks to reconstruct the process by which primitive cells—that is, life—emerged from a swirl of chemicals some 4 billion years ago.

### HENRI TERMEER

**cofounder | Lysosomal Therapeutics**
**Cambridge, Massachusetts, U.S.**

In a 2013 article, *The Boston Globe* called Termeer "a life sciences legend." Termeer served as chairman, president and CEO of Genzyme, a company that he ran for nearly 30 years. He sits on more than a dozen biotech boards and continues to mentor people entering the field.

### SHIRLEY TILGHMAN

**professor | molecular biology | Princeton University | Princeton, New Jersey, U.S.**

"I have been worried for some time that the improvements in the status of women in our society have slowed in recent decades, after remarkable gains in the wake of the feminist movement," Tilghman recently told *The Daily Princetonian*. "It is very clear that until we find better solutions for working parents—including paid maternity leave and proper child care options—the progress is going to be slow."

### LUKE TIMMERMAN

**founder & editor | *Timmerman Report***
**Seattle, Washington, U.S.**

"Many biotech companies have overreached on drug pricing," Timmerman asserted. "The industry could go a long way toward restoring public trust by lowering prices, or at least backing off on the relentless increases. Public reputation matters for a number of reasons. Public funding is essential for the basic research that helps advance industry. Biotech also needs a large pool of people willing to participate in clinical trials, and share their health data. People are reluctant to do those things for people they don't trust."

### ERIC TOPOL

**director | Scripps Translational Science Institute | La Jolla, California, U.S.**

Topol said his chief contributions to biotech have been the new drugs he has helped develop, such as tPA and abciximab (ReoPro). These medicines, he noted, are "now expanding across all medical disciplines and diseases" and have "completely changed the landscape of effective treatments."

### ROBERT URBAN

**head | Johnson & Johnson Innovation**
**Boston, Massachusetts, U.S.**

"This moment in medicine is really a very exciting demonstration of how converging talents can be leveraged," Urban said in a video produced by the Science & Technology Innovation Program at the Woodrow Wilson International Center for Scholars. "The biologists who understand the molecular basis of disease in unprecedented ways are beginning to work more closely with technologists and engineers to [turn] that knowledge into a form of know-how that can [lead] to new types of products that can be used by physicians."

### MARC VAN MONTAGU

**founder & chairman**
**Institute of Plant Biotechnology Outreach**
**Ghent University | Ghent, Belgium**

"I want to stress that this GM technology we developed in Ghent, that it's really technology that we needed," Van Montagu told the audience at TEDx in 2014. "So it's a myth that is propagated that we can do without."

### FLORENCE WAMBUGU

**CEO | Africa Harvest Biotech Foundation International | Johannesburg, South Africa**

"Our mission is to improve food security and the welfare of African populations by using the tools of agronomy and agricultural biotechnology," Wambugu recently told the Life Sciences Foundation's *LSF Magazine*. "We are working to build healthy communities and help smallholder farmers produce plentiful, nutritious food supplies…. We are working to create sustainable agricultural systems."

### JUDY WANG

**senior manager | biotech affairs & regulatory**
**DuPont Pioneer China | Beijing, China**

"I personally have been engaged in biotech R&D and management since 1996," Wang wrote in a response on GMO Answers. "I have seen [the China Ministry of Agriculture] grant Safety Certificates for importing food and feed processing material from biotech crops….In 2012 alone, China imported 58 million tons of biotech soybean and became the world's biggest country for biotech soybean importation and consumption."

### JAMES WATSON

**chancellor emeritus**
**Cold Spring Harbor Laboratory**
**Cold Spring Harbor, New York, U.S.**

While heading the Cold Spring Harbor Laboratory, Watson commissioned the DNA Learning Center (DNALC) in 1987 to deepen the public's understanding of DNA, the genome and related technologies. Since that time, the DNALC has provided hands-on training for introducing students from middle school through high school to molecular genetics. The program has reached half a million kids on Long Island and in New York City, along with tens of thousands of teachers, who received instruction on teaching biotechnology-based lab units and even entire courses.

### MARY WOOLLEY

**president | Research!America**
**Alexandria, Virginia, U.S.**

Discussing the 21st Century Cures legislation in one of her weekly advocacy messages, Woolley wrote: "Among our priorities will be to ensure that basic discovery is not neglected….We will continue to push for final bipartisan language that effectively boosts the return on medical progress by accelerating discovery, development and delivery."

### TADATAKA "TACHI" YAMADA

**executive vice president, chief medical & scientific officer | Takeda Pharmaceuticals**
**Osaka, Japan**

If he hadn't entered the field of biotechnology, Yamada said, "I think I would still have focused on patient benefit by pursuing my career as an academic physician or as someone committed to global health." Of the past year's biotech advances, he found "the maturation of gene therapy and microbiomics as real market opportunities" the most intriguing.

### SHINYA YAMANAKA

**director & professor**
**Center for iPS Cell Research & Application**
**Kyoto University | Kyoto, Japan**

Yamanaka received the 2012 Nobel Prize for his invention of induced pluripotent stem cells (iPSCs). Writing on the Knoepfler Lab Stem Cell Blog about the rapid pace from discovery to use of iPSCs in a clinical trial, he said: "The rapid transition is because many bright and passionate 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."

### GEORGE YANCOPOULOS

**president | Regeneron Laboratories**
**Tarrytown, New York, U.S.**

"Innovation in science and technology is at the heart of Regeneron's mission to discover and develop new treatments for serious diseases," Yancopoulos said while discussing the 2014 Regeneron 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."

### ELIAS ZERHOUNI

**president, global R&D**
**Sanofi | Paris, France**

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

### DAPHNE ZOHAR

**founder & CEO | PureTech Ventures**
**Boston, Massachusetts, U.S.**

"Our industry is very good at pattern recognition," Zohar told *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 alone 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," this page). Then, a look inside LabCentral's "launchpad" for bioentrepreneurs (page 26) and an essay by industry expert Stephen Sammut (page 28) attest to the countless ways people in our field get together to nurture the evolution of ideas into commercial products. As these stories illustrate, this process often takes a number of complicated, yet fascinating, turns along the way.

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# FROM *EUREKA* TO USEFUL

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

For 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 school vacations, though, Ntseoane's mother would take her and her brother to a farm where her uncle worked. "As a child I hated every first few days of the visit, but with chickens and puppies around, I would start enjoying it," she remembers. "One morning my cousin and I climbed on the wagon carrying farmworkers to the corn fields. It was fascinating to help out, though we played most of the time."

Ntseoane studied agriculture during her first three years of high school, but she says, "It came with a stigma that farming was for the not-so-clever." Eventually, she succumbed to the peer pressure and her parents' wishes, and became 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 for the Vaal Dam that supplies water to most South African provinces," she says.

She began farming corn, working with traditional varieties. But in 2011, she says, "AfricaBio, an organization in South Africa, introduced me to Bt maize." This corn gains insect resistance through a bacterial gene derived from *Bacillus thuringiensis* (Bt) that encodes a toxin. When Ntseoane planted these seeds on two hectares, they produced 7 tons of corn per hectare. That was more than double her previous harvest of conventional corn, which, at 2 to 3 tons, was kept at a low yield by stalk borers. The next year, the Bt corn again produced 7 tons per hectare for Ntseoane. Even in the following draught year, every hectare of the Bt corn yielded 5.5 tons. As Ntseoane says, "Had I not used the new technology, I wouldn't have harvested much."

Ntseoane's story illustrates a fundamental truth in the field of biotechnology: getting the most out of a technical innovation requires vision, courage and commitment—plus the ability to take advantage of available resources.

## ACCELERATING INNOVATION'S APPLICATION

"Innovation is the creative lifeblood of every country," wrote The Honorable Birch Bayh in the forward to Michael A. Gollin's *Driving Innovation*. Many would argue that the same could be said for the complex and promising field of biotechnology.

The question is: How can scientists turn "eureka moments" into useful products and services more quickly, more effectively? In *Think Like a Freak*, Steven D. Levitt and Stephen J. Dubner write: "The modern world demands that we all think a bit more productively, more creatively, more rationally; that we think from a different angle, with a different set of muscles, with a different set of expectations; that we think with neither fear nor favor, with neither blind optimism or sour skepticism."

In addition to that new kind of thinking, would-be innovators must also learn from experience. As Levitt and Dubner point out, "The key to learning is feedback. It is nearly impossible to learn anything without it." And when gathering feedback, it never hurts to turn to the best and the brightest, like Robert Langer, the David H. Koch Institute Professor at MIT and the author of over 1,000 patents, which have been licensed to more than 300 companies.

> 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. I like it to be based on breakthrough science that could be really game-changing." And when assessing the way forward—from the discovery in the lab to working toward commercialization—he warns against a common mistake: underestimating the task. "The major thing people do is underestimate how long it takes, how expensive it is and how many difficulties you'll run into." In order to combat these issues, he encourages biotech entrepreneurs to be prepared. "Surround yourself with great people," he 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 their own work down this road, and he says, "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. But when Jobs took over again, it rose to become the world's most valuable company. The lesson, Langer stresses, is that even the most astoundingly innovative ideas need the leadership of a champion to succeed.

## MAKE 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,

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

"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 someone creates 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 Sweden's Mentor4Research program, 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 Mentor4Research advisor. "Still, we understood that the NGS market was growing tremendously." Nordström helped Ericsson structure the approach, make important contacts and build a company called Halo Genomics—which Agilent Technologies soon acquired—that eventually turned the innovation into a product called HaloPlex. As Nordström recalls, "We knew we were in a very hot market."

For most innovators, however, the road ahead is rarely that clear. Typically, says Nordström, "You have to start with assumptions, and then try to validate them through a network of experts. From that, you can see if the assumptions sound reasonable or not." Building a community of advisors helps scientists test these assumptions (see "Room to Grow," page 26).

Start-up expert Steve Blank, architect of the U.S. National Institutes of Health's I-Corps @NIH program, which teaches scientists and clinicians how to take their biotech ideas from lab bench to bedside, agrees. "We now understand that innovation in life sciences requires two parallel paths," he says. "First, making the science better and useful. But second, we need to understand how to commercialize the science. We never had a formal process to test whether the science could turn into a commercially successful product. We do now."

The I-Corps/Lean LaunchPad methodology, which Blank developed, allows for rapid testing and learning. "People hypothesize in the lab but rarely think of things like 'Who do you think will pay for this?'" he explains. To find out, Blank makes scientists in the program go out and talk to at least 100 potential customers. "The principal investigators must get out and see the people," he says. "For one thing, you might find that the market wants something that you have but that you thought no one would want."

> The biggest mistake is thinking that your faith is fact.

What are the most common mistakes made in turning an innovative idea into something commercial? "The biggest mistake is thinking that your faith is fact," says Blank. The I-Corps @NIH addresses that problem when it makes an innovator take an idea to the real world. "You start with faith in your idea and then replace as much of that with fact as soon as possible," he says.

Making the right assumptions about the market, however, solves nothing without the right science. Sean Ainsworth—now CEO of RetroSense Therapeutics in Ann Arbor, Michigan—learned that the hard way. "In a previous company," he says, "we were working on a science that hadn't been as fully validated as it needed to be." And unfortunately, the company was already raising capital and lining up customers when obstacles in its research turned up. "We returned the money to the investors," Ainsworth says, "and we took the science back to the lab."

That experience made Ainsworth extra cautious with RetroSense—a company with a gene therapy that repairs vision in people with retinitis pigmentosa or age-related macular degeneration. "We ensured that it wasn't just one individual who had developed and published something," he says. "In this case, it had been done with people around the world." With solid research in place, RetroSense has continued to thrive. In fact, it recently raised US$6 million to file an investigational new drug (IND) application with the U.S. Food and Drug Administration (FDA).

## SPREAD THE CAPABILITIES

Indeed, developing an innovative product and finding a market for it is a challenging feat under the best of circumstances. But, not surprisingly, in some areas of the world it is far easier than in others. As the founder and CEO of Seeding Labs in Boston, Massachusetts, Nina Dudnik sees this disparity firsthand. Her organization works to bring advanced scientific instruments and training to developing countries. When asked if scientists in developing nations suffer more from a lack of the tools needed to innovate or from a need for the means to commercialize their innovations, Dudnik points out that the two are inextricable linked. "There are obstacles at every point along the way," she says. "For the scientists we serve, the first barrier is usually related to a lack of access, not potential. Without access to the tools and infrastructure needed to make discoveries, the potential to innovate based on that research is severely diminished." Which is exactly why Seeding Labs is committed to providing that access. For the moment, the dearth of equipment seems to be the dominant concern in developing countries. As Dudnik says, "From my observation, the difficulty in obtaining

« Seeding Labs sends scientific equipment and expertise to developing countries.

resources for research itself overshadows the focus on taking the discoveries out of the lab and into the market."

Helping these nations become biotech innovators who can get their 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 Worldview* 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 nonprofit 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."

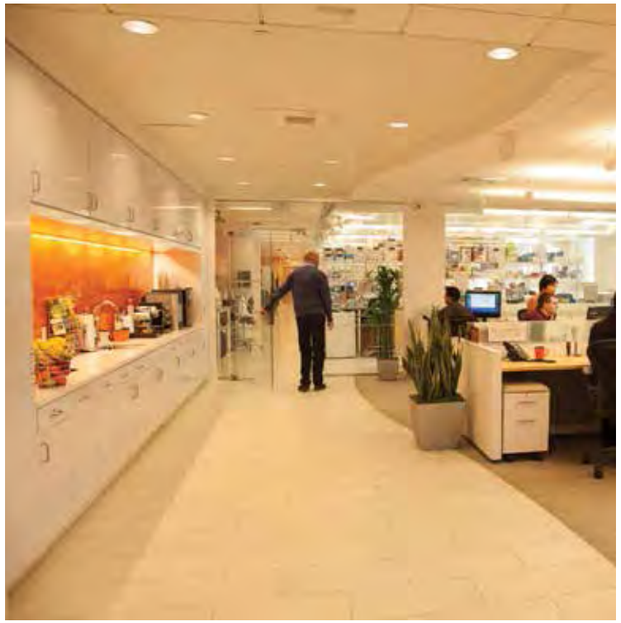
The "other funders" in Sweden, and most other countries, provide venture capital (VC). To gain a better understanding of how biotechnology VC works in Sweden, *Scientific American Worldview* talked with Eugen Steiner, CEO of Glionova Therapeutics in Stockholm and a venture partner for HealthCap, a family of VC funds investing in international life science research. In addition, Steiner has served as the CEO for several small start-ups.

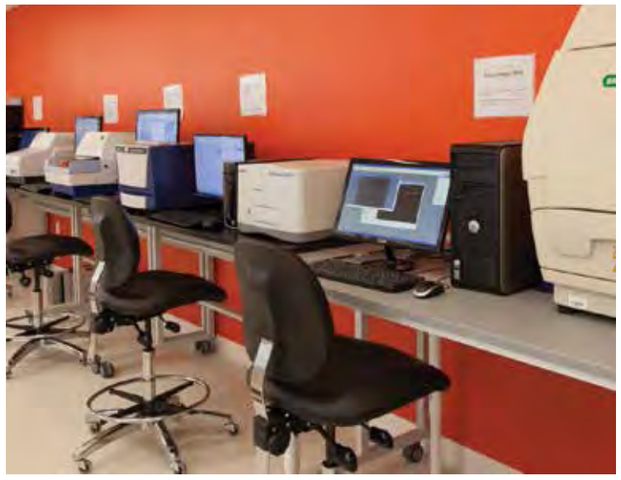
Although he admits his bias as a partner in a VC firm, Steiner says, "There would be no biotech industry if there were no VCs." Biased or not, few in the field would disagree with Steiner's blunt assessment, because it takes money—often lots of it—to commercialize an innovation.

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 fledgling 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 tend to be further along, and in troubled economic times, they're the ones that get the VC. Such is the law of the VC jungle.

And while being 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 Ntseoane'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.



# ROOM TO GROW

*LabCentral gives start-ups the space and resources to thrive* **BY JOHANNES FRUEHAUF**

In 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 Biolabs 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 Biolabs 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 in Cambridge. Over time, we leveraged that funding to bring in nearly $20 million in additional commitments of cash, state-of-the-art equipment and in-kind services.

## FILLING A VOID

Biotech start-ups need lab space and resources to test out, challenge 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. 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 learn" programs, big-screen movie and sports-viewing parties, and social- and business-networking events.

## RAPID UPTAKE

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.

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.

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 eschew that term. It suggests that biotech 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 $200 million in venture capital and other sources of funding. That's about the same amount of venture capital raised by all of Switzerland's biotech companies in 2014.

## EARLY RETURNS

Providing biotech entrepreneurs with a fertile environment with the best infrastructure, equipment, services and programming to enable their unfettered practice of science on day one is LabCentral's *raison d'être*. Already, LabCentral is at the center of the Kendall Square bioinnovation ecosystem, which fosters collaboration and creative exchange of science and business ideas among our entrepreneurs and the countless scientists, thought leaders, industry experts and potential funders who work at the academic- and industry-research institutions, venture firms, law practices and equipment/service suppliers nearby.

The LabCentral environment provides tremendous flexibility that spurs innovation. As Michael Schrader, cofounder and CEO of Vaxess Technologies, explains: "LabCentral has allowed us not to expend a ton of money for equipment or long-term leases. As we look to expand, we have grown our network of contacts tenfold through the collection of companies at LabCentral, compared to operating on our own. We love the facility, the open floor plan and comingling with other teams who are not directly competing with our science, but rather complementing it— facing the same challenges in fundraising, science and business development, from whom we can learn and with whom we can share to the benefit of all."

Schrader's neighbors agree. "LabCentral makes it as easy to start a biotech company as it is to start a purely IT company," says P. Shannon Pendergrast, cofounder and chief science officer of Ymir Genomics. "It provides the critical infrastructure, including sophisticated scientific equipment bio-innovators need to excel." Most important, he adds, it allows Pendergrast and his fellow bioentrepreneurs the freedom to focus on the work at hand: "All I have to do is science."

***Johannes Fruehauf is the president and executive director of LabCentral. For more information, visit www.labcentral.org.***

# BIOTECHNOLOGY'S CRUCIAL QUESTION

*In this industry, what matters the most: technology or people?*

**BY STEPHEN M. SAMMUT**

The reflexive answer to this question is most likely: the technology. Without a new method, cure, device or something that makes a difference in the lives of people or communities, there has been no progress. As true as that rings, there is at the very least a codependence of the underlying technology and the people who turn it into reality. Some might argue—myself included—that the biotechnology industry is entirely people driven and enabled. The very definition and realization of a product needs definers and builders who know how to find and marshal the necessary intellectual, managerial and financial capital to make things happen.

The human resources biotechnology demands fall into four broad categories:

***Scientific and technical.***
This includes the Ph.D.s and other graduates in the life and medical sciences, whether they be recently minted or with decades of experience in the industry. The production of life and medical Ph.D. scientists has largely been addressed in most countries throughout the world. Whether there are an adequate number of academic or industrial positions for these scientists is a question that is beyond the scope of this article.

***Managerial & administrative.***
This category consists of the people educated or experienced as strategic thinkers, organizers and coordinators of either academic or commercial enterprises. In biotechnology, many of the people in this category were trained as scientists and moved from the bench to the boardroom. While there are some forward-thinking academic programs that combine Ph.D. studies in the life sciences with MBA studies, managers in biotechnology usually emerge either from the marketing side of the biopharma industry or from the laboratory where they have accrued successive responsibilities in research management. These managers are necessary for the success of an existing organization, but insufficient to drive the "new."

***Entrepreneurial founders.***
Although these people make up a subset of scientists, managers or a combination of the two, it is best to break them out into a separate category, because the risk affinity—or tolerance—of the entrepreneur is typically the starting point of new venture creation in this industry and all others. Entrepreneurs possess a combination of native skills, education, experience and personality traits that put them in a category of their own. Some are aware early in their careers that entrepreneurship is their career destiny. Others discover their inner-entrepreneurship tendencies after years of commercial responsibilities that build their confidence and hone their skills.

***Entrepreneurial enablers.***
The entrepreneurial academic literature implies, but seldom studies, this category. Entrepreneurial enablers are the experienced managers of functional areas—such as technology and information management, strategy and marketing, finance and operations—who have the risk tolerance and drive to make something new happen, but who might not independently 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 respective 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 that, 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 leanings? It means there must be 15,000 entrepreneurial founders. If each company needs, say, six entrepreneurial enablers, that would compute to a total of 90,000 of them worldwide. So, overall, the industry requires 105,000 bio-entrepreneurs.

Beyond the numbers, these leaders have to possess many capabilities:

*Leadership:* formulate human resource needs and manage the hiring and development of teams.

*Strategic thinking:* make choices based on alternatives and options.

*Tactical planning:* organize resources to achieve strategic ends.

*Technology assessment:* manage a team that can review scientific 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 technology-driven product to meet unmet customer and commercial needs, compete with alternatives, achieve a level of pricing that justifies the investment and assures sustainability, and that can be promoted with a clear, distinct, 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 intellectual property assets internationally and domestically through a variety of strategies, including licensing and partnering.

*Capital formation, replenishment and stabilization:* define capital requirements and sources over long time periods, and accumulate the financial resources necessary to meet the development and commercial objectives of the company.

*Communication management:* encapsulate the mission and methods of the company into a succinct and persuasive message in order to attract human resources, build internal consensus, drive strategy and operations in an organized fashion, assure stakeholders that the company is mindful of the totality of challenges and obtain needed financing.

*Impact management:* marshal the assets and resources of the company towards defined needs in an ethical manner that delivers the greatest good to the greatest number of people.

> Teaching can be developed to provide new entrepreneurs and entrepreneurial enablers with a toolbox for orienting their thinking and laying a groundwork for immediate action as well as long-term study.

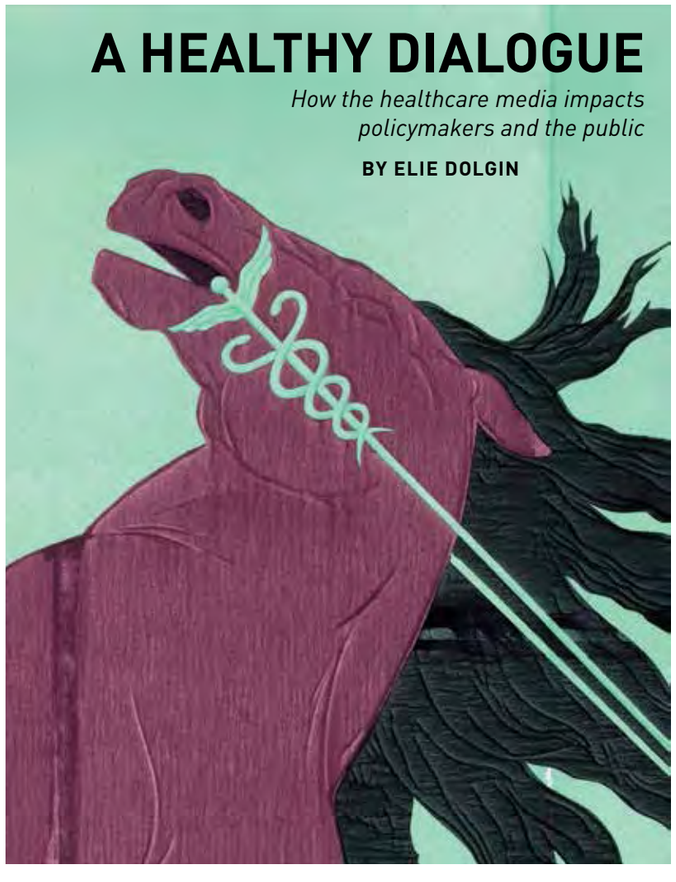
This knowledge comes from formal training and experience. Although it is unreasonable to expect that an intensive approach to imparting the associated insights would ever compete with disciplined study over years or the lessons associated with making day-to-day and strategic choices, teaching can be developed to provide new entrepreneurs and entrepreneurial enablers with a toolbox for orienting their thinking and laying a groundwork 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 experiences 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.***

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 its ability to clearly convey its strengths and objectives. More important, if the media gets a story wrong, the general population may face undue health risks as a result.

Indeed, it's crucial to get communication right in biotechnology, and, as the following stories demonstrate, that's not always easy to do.



# A HEALTHY DIALOGUE

*How the healthcare media impacts policymakers and the public*

**BY ELIE DOLGIN**

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On a Saturday night in November 2009, Canada's most-watched television network, CTV, ran a primetime documentary that would radically change the country's healthcare landscape. The *Globe and Mail*—a popular Canadian newspaper and part of the same media conglomerate—carried a companion story on its front page.

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 contended 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 constriction created a build-up of iron that, in turn, set off the cascade of inflammation and nerve degeneration that are the hallmarks of the disease. Zamboni advocated a treatment similar to balloon angioplasty. He even tested the surgical intervention on his MS-afflicted wife and, as the CTV documentary displayed, her symptoms seemingly melted away. The treatment, nicknamed the "liberation procedure," was touted as a miracle cure.

It was a powerful and emotional story, but scientifically unfounded. The media coverage—based only on the most preliminary of Zamboni's findings—spurred "an over-enthusiastic and inadvertent promotion of some shaky science," André Picard, the *Globe and Mail* journalist who coauthored the original newspaper story on the procedure, wrote in *BMC Medical Ethics* in February 2013.

After the initial reports made the rounds on the Internet, the public started demanding that health authorities make the procedure available in Canada. The media coverage snowballed, prompting an unprecedented amount of political involvement in the allocation of research funding. Federal and provincial legislators pledged millions of dollars to support clinical studies. That research, however, failed to confirm Zamboni's hypothesis. The liberation procedure proved ineffective and possibly 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 reporting might have an increasingly large influence on medical research and healthcare.

**The Zamboni escapade was not the first time that a scientific claim hyped in the media turned out to be wrong.**

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 importance 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 Schwitzer, founder of the watchdog website HealthNewsReview, traditional media sources are still routinely disseminating misleading health information. Schwitzer and a team of reviewers looked at about 1,900 health-related stories about drugs, medical devices or other interventions published by U.S. news organizations between 2006 and 2013. As Schwitzer reported in July 2014 in *JAMA Internal Medicine*, most of the stories overplayed benefits, minimized harms and ignored discussions of cost.

This kind of poor reporting can have real-world consequences. For example, after U.S. regulators issued health advisories about a slightly increased risk of suicidal thoughts and behavior in young people who take antidepressants, widespread media coverage spurred a dramatic decline in antidepressant use. According to a study published in *BMJ* in June 2014, this had an unintended consequence: suicide attempts increased among adolescents and young adults, most likely due to an under-treatment of serious mental health disorders. "The sexy story isn't 'Be cautious and think carefully about medicines,'" says psychiatrist Steven Schlozman, associate director of the Center for Mental Health and Media at the Massachusetts General Hospital in Boston. "The sexy story is 'These medicines might kill your children.' There's not much of a story if you report it in nuanced tones."

## Pushing Prescriptions

More often, press coverage leads consumers toward increasing healthcare utilization—sometimes even for problems they might not have. In a phenomenon known as "disease mongering," pharmaceutical companies have even co-opted the media to convince people that they are sick and in need of medical treatment.

Such was the case with restless legs syndrome. Lisa Schwartz and Steven Woloshin from the Dartmouth Institute for Health Policy and Clinical Practice in Lebanon, New Hampshire, analyzed the media stories written in response to press releases in the mid-2000s from GlaxoSmithKline, the company behind the first drug approved for the syndrome. As the researchers reported in *PLoS Medicine* in April 2006, most journalists uncritically reported GlaxoSmithKline's claims, encouraging more diagnosis and treatment. "Many of the stories that we looked at sounded like company press releases," says Schwartz. In a 2013 article in *JAMA Internal Medicine*, she and Woloshin documented similar campaigning through the media to promote hormone-replacement therapy for low testosterone in men—now a multi-billion-dollar industry.

Beyond sloppy reporting, part of the problem could lie in the financial ties between medical journalists and drug companies. Wendy Lipworth, a bioethicist at the University of Sydney, has studied this issue in Australia. She thinks that more disclosure is needed on the part of journalists and that some kinds of monetary relationships should be banned. But, she concedes, it might be difficult to implement these remedies in an increasingly fractured media landscape.

It's not just journalists who are to blame, though. A December 2014 study in *BMJ* from Petroc Sumner of Cardiff University found that press releases from the UK's leading research universities often made their own overblown claims and unwarranted inferences about health studies. Scientists usually vet and approve the press releases issued by their institutions, and thus must shoulder some of the accountability for the inaccuracies and exaggerations that creep into stories about their research.

In the end, everyone carries some responsibility—from the media consumers hungry for miraculous cures to the companies seeking profits, and everyone in between. As Sumner says, "All of us are not watchful enough."

## BREAKING THE BAD-GUY IMAGE

*Johnson & Johnson's Seema Kumar urges companies to stay transparent*

"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 the important translational research that goes on in industry 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 well-being." Despite what she considers 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—industry's 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 research through the Yale University 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—journalists and corporate science communicators—can do to showcase how important science is to society, the more it will benefit all of us in building a scientific powerhouse, an innovative country."

**—MIKE MAY**

# COMMUNICATION BREAKDOWN

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

Despite decades of globally expanding use of genetically modified (GM) crops, broad public acceptance still eludes this technology. The history of the dialogue behind these crops, however, reveals what we can learn from communications science.

Over the past 20 to 30 years, the world has changed considerably, with populations becoming aware of the risks in their everyday lives. Consequently, people in general have grown more averse to risk. With health scares in food and agriculture, like mad-cow disease in the United Kingdom and melamine in infant formula in China, people around the world have started losing trust in the people and organizations that regulate the risks.

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 from a communications standpoint. 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 Teng, chairman of the International Service for the Acquisition of Agri-biotech Applications (ISAAA), said: "Communication is key for GM product acceptance, but just sharing information alone is not sufficient. Infusing values into communication messages will contribute greatly to making GM products part of everyday life."

Still, some groups try to get across those messages with techniques that are known to be flawed. For instance, creating "independent" third-party organizations to deliver the message—a common technique among agencies retained to advocate for GM crops—has been widely questioned at high levels. In a 2013 speech, for example, Margaret Chan, director-general of the World Health Organization, provided insight into the tactics of large regulated industries—big food, big soda and big alcohol—and said: "They include front groups, lobbies, promises of self-regulation, lawsuits and industry-funded research that confuses the evidence and keeps the public in doubt."

Likewise, the use of so-called credible experts, largely appointed for their technical expertise, has lost much of its value, yet it remains at the top of the list of approaches to communications about GM crops. Even worse, some groups have tried putting a modern twist on the tactics of big tobacco in 1950s and '60s, such as creating fake online grassroots groups and identities extolling the virtues of GM crops. It's hard to imagine what could do more harm to earning trust.

## 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 concerns them, rather than the "technical" hazard itself. Peter Sandman, one of risk communication's pioneering 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 reframe the issues in terms of technical expertise and experience, 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 do far more to safeguard the public trust, especially in complex cases that often hinge around degrees of uncertainty.

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Many factors conspire to make the acceptance of GM crops difficult. Nonetheless, communicators in biotechnology, especially in North America and Australia, now accept the need to address the cultural values that come into play in communicating 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 cognition theory of risk communication for GM crops that aims to deeply assimilate cultural values into a process not aimed at acceptance, but aimed 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 research to gain further insights into the groups with which we are communicating. As a result, we will learn to understand existing and new concerns—not just about GMOs, but also about all areas of innovation. When there are 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.

***Andrew D. Roberts and Andrew D. Powell are, respectively, COO and CEO of Asia BioBusiness Pte Ltd. in Singapore and cofounders of the Centre for Risk Communication Asia.***

# First Came Access Now Comes ACTIVATION

## A New Category of Innovation – Just In Time for Precision Medicine

The irony of our modern era, where precision medicine, 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 not 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, leveraging every possible avenue toward the best care options possible for their very specific diagnosis and minimizing the chance of any potential treatment slipping through the cracks.

The ultimate goal of our medical ecosystem is to identify the causes of disease and proceed with the most effective treatment as efficiently and timely 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, unavailable or simply unknowable is a source of frustration and sometimes hopelessness.

We all know too well, whether personally or through family members, the anguish of receiving a difficult diagnosis of a deadly disease. Even in an era of boundless health information, digital connectivity 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? Are there clinical trials available as an option for me to explore? How do I even do that?" This questioning and trying to find relevant information quickly can, in short order, become daunting, time consuming and ultimately frustrating.

***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.***

**ENTER CURE FORWARD, A PATIENT ACTIVATION COMPANY.** Cure Forward is leading the way towards innovative health solutions that put 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.

Leveraging the power of science and the power of community, Cure Forward seeks to provide a 360-degree approach for the entirety of the medical ecosystem, and offer a sum much greater than its parts, combating disease, creating efficiencies and opportunities, and reducing that ominous feeling in the pit of patients' or their family members' stomachs. It is truly the first **Patient Activation Company**.

In the same way multi-sided technology platforms proactively connect relevant stakeholders to produce value for all parties, much like Airbnb or Kickstarter, Cure Forward will enable patients, with complete anonymity and privacy, to access their molecular data (a tumor profile), understand it through educational tools, connect with patients across the world with similar conditions, and give the patients the ability to seek out clinical trials in a simple way without having to have an advanced degree to understand the complexities of the trial requirements. A patient does not have to trawl endless trial descriptions or fear they won't connect to all of the information available. Innovative new therapeutics can quickly find their beneficiaries through an activated patient network. And communities, created around specific disease states, molecular profiles and other criteria, will be valuable sources of support, information and timely input.

## THE MANY AUDIENCES AND VALUES OF CURE FORWARD:

**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 lab doesn't make results available 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 apply to their trials. 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 faced with 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 will use Cure Forward to find tests that may be relevant to their care, Cure Forward is a potent marketing channel for diagnostic laboratory partners (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 understood. Cure Forward can answer many of the basic questions that otherwise might be handled by the testing laboratory. Consumer-level customer support 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 transformational therapies are proven. But it can take 2–3 years to fill a targeted trial, and more than half of trial sites fail to accrue a single patient! 85% of patients don't know that clinical trials are an option to consider, yet 75% say they would seriously consider a trial if it were available. Patients in the community setting are simply not visible to trial sponsors until they apply for entry, and too often those applications never come. 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 a scientific problem, Cure Forward aims to increase patient participation in clinical research, to help individuals gain access to new therapies and to help those 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, broad, precise, low-cost recruiting, and pay-for-performance economics. This is a new way to accrue clinical studies.

**Learn More -**
To learn what a Patient Activation Company is all about, and to see how innovation can better serve every part of the medical ecosystem, please visit:

**www.cureforward.com**
Beta release begins in June 2015

## *SCIENTIFIC AMERICAN WORLDVIEW* SCORECARD

Our Scorecard analyzes and interprets data on the innovation potential in biotechnology for 54 countries. Based on seven Scorecard Categories—created from 27 components—this analysis combines information from biotechnology inputs and outputs through government protection and policies and far beyond. The results reveal the dramatic range of capabilities in this dynamic field, and which countries are moving ahead and which ones are falling behind.

To get the most from this analysis, work your way through the introduction and Scorecard Categories on your way to the Overall Scores ahead. Beyond that, finer-grain analyses add even more depth to our understanding of the innovation potential in biotechnology around the world.

**Start exploring!**

# POWER POINTS

**Which places around the globe are powering the success of biotech today?**

2015

10

*Our Scorecard pinpoints the countries, communities and financial sources that enable innovation to flourish*

## 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.

As in the past, we built the Scorecard using a diverse collection of metrics—from education and political environment to intellectual property strengths and the performance of public companies. To quantify this information, we ranked each country's achievement on a series of individual components using a scale from 0 to 10, with the lowest-ranked nation scored as 0 and the highest-ranked as 10. We then generated scores for each category—Productivity, Intellectual Property (IP) Protection, Intensity, Enterprise Support, Education/Workforce, Foundations, and Policy & Stability—by calculating the mean score of these components. (For detailed methods, see page 46.)

Our analysis of gross and relative metrics provides a rich assessment of the biotechnology sector worldwide. The results reveal a number of surprising shifts in the industry, as well as several unexpected players exceling in certain areas. As the biotech field continues to evolve, so do our methods for tracking those places around the globe where today's innovators have the best chance of bringing tomorrow's innovations to the fore. **—THE EDITORS**

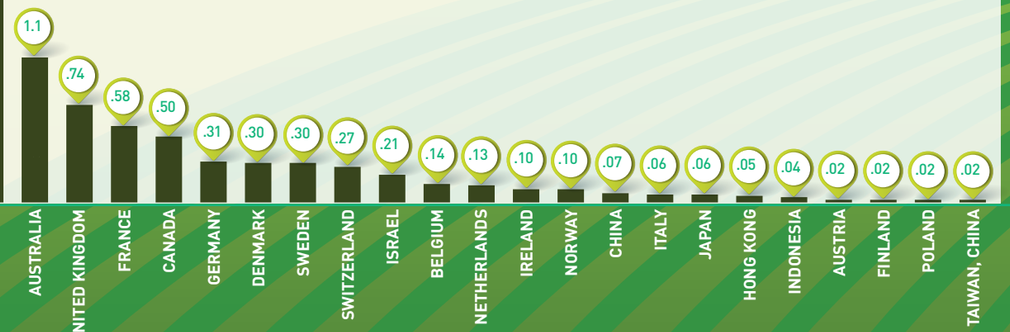
SCORECARD CATEGORY #1:

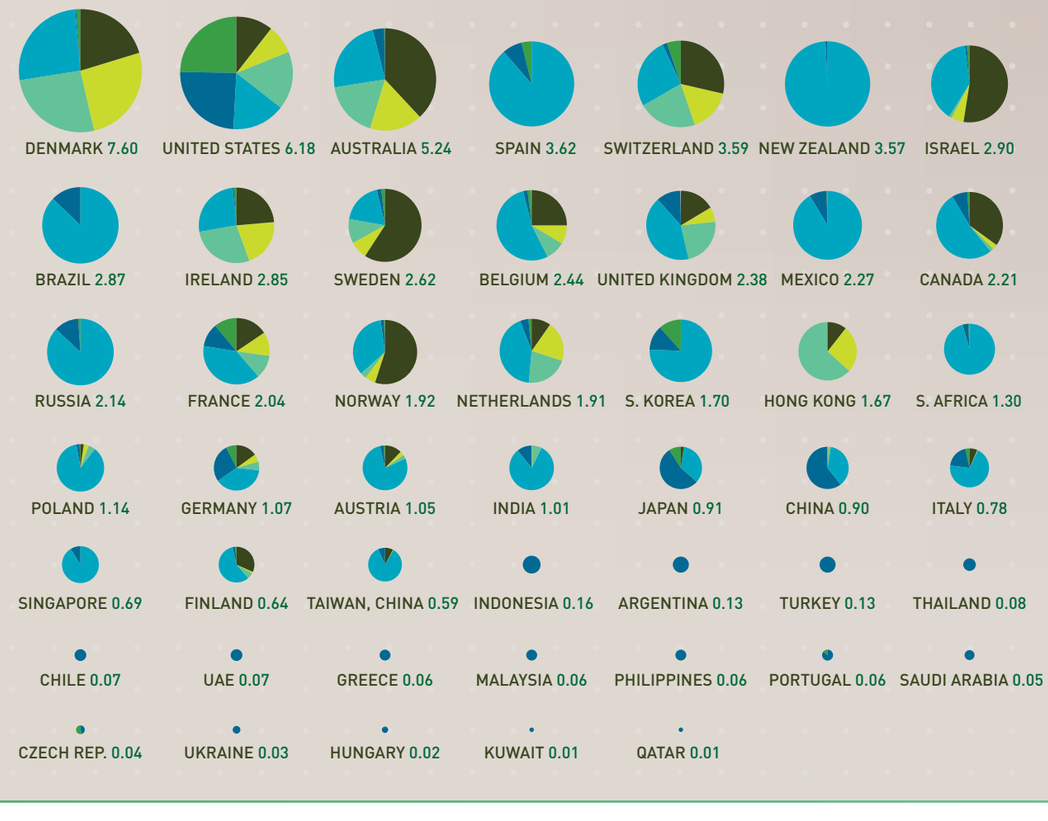
## PRODUCTIVITY

*In overall output, no one comes close to the U.S.*

Although a country's capabilities in biotechnology depend on many factors, perhaps the most important is gross productivity. Innovation is not worth much if it cannot be commercialized, and that's what our **Productivity** category measures. We compute productivity using two metrics: "public company revenues," and the "number of public companies" (Lawrence, S. & Lähteenmäki, *R. Nat. Biotechnol.* **32**, 626–632 (2014), and company disclosures). We favor public companies because—relative to private firms—their reporting requirements provide transparency, making it easier to compare them objectively. Further, it stands to reason that a nation with a favorable business climate will support the development of more public companies. In combination, these metrics assess a country's productivity.

The United States—the longstanding leader in this category—remains at the top. In fact, the U.S. runs away with this metric, finishing well ahead of all competitors. Australia and the United Kingdom follow in second and third place, respectively, as they did last year, but far behind the front-runner.




SCORECARD CATEGORY#2:

## 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 **IP Protection**. Without that assurance, it is difficult to attract funding or convince ambitious scientists and business founders to take on the risks of pioneering research and development.

In addition, IP protection can encourage foreign development of medicines for domestic needs. 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 Worldview*, 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, and that the perception of a country's IP protection might not match objective measures, we account for subjectivity with Schwab's "perceived IP protection" metric (Schwab, K. *The Global Competitiveness Report*, 2014–2015. World Economic Forum (2014)). 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 in 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.

SCORECARD CATEGORY #3:

## INTENSITY

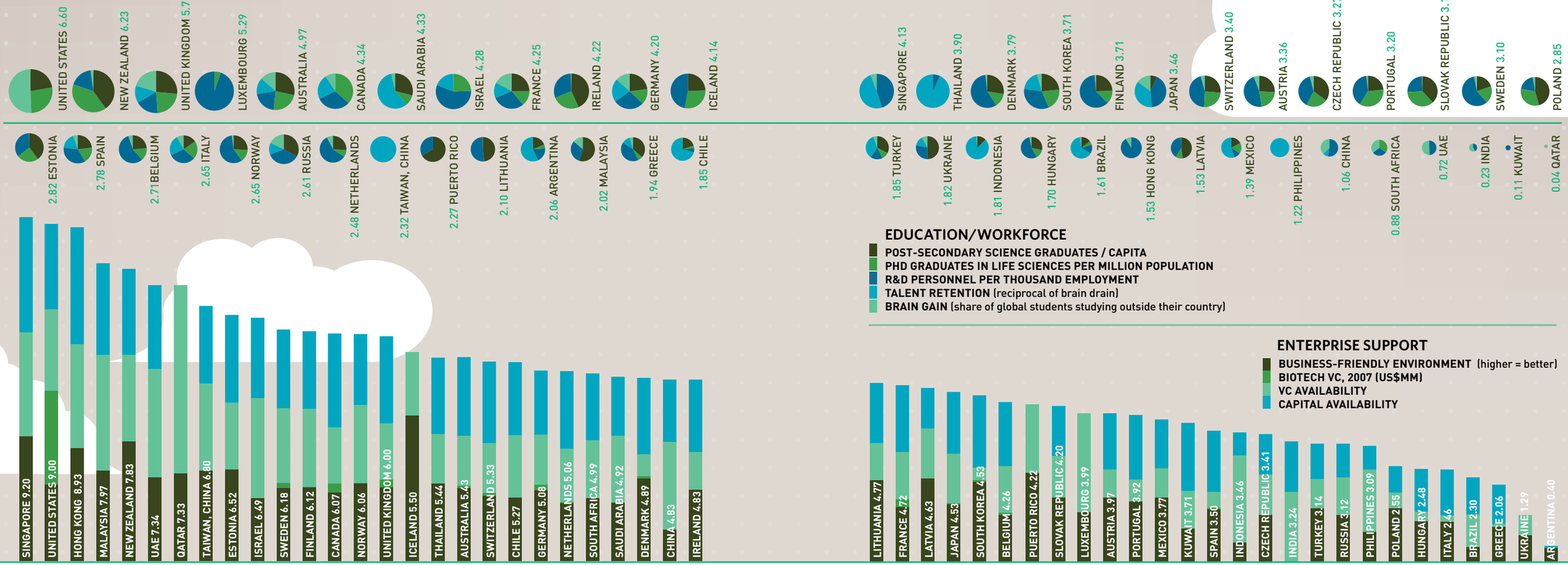
*Top marks for Denmark in driving innovation*

- PUBLIC COMPANIES / MILLION POPULATION
- PUBLIC COMPANY EMPLOYEES / CAPITA
- PUBLIC COMPANY REVENUES / US$B GDP
- BIOTECH PATENTS /TOTAL PATENTS FILED WITH PCT
- VALUE ADDED OF KNOWLEDGE- AND TECHNOLOGY-INTENSIVE INDUSTRIES

We measure a country's overall efforts to boost biotech innovation by combining five characteristics into a measurement designated as **Intensity**. These characteristics are normalized for population size and overall economy. As a result, Intensity helps identify smaller nations that exhibit outsized activity in the sector. Whereas Productivity measures outputs, like commercial products, Intensity measures inputs—the elements that propel companies to success. Those looking for research partners or a place to develop biotechnology should consider countries with high Intensity scores.

The data used in the components of Intensity are gathered from various sources, including company disclosures and published information (Lawrence, S. & Lähteenmäki, *R. Nat. Biotechnol.* **32**, 626–632 (2014)). For instance, dividing each country's employee counts by its population, as sourced from the U.S. Census Bureau International Database, produces the "public biotechnology company employees per capita" metric. Likewise, the measurement of "public biotechnology company revenues per GDP" is generated by dividing a nation's Productivity score by its GDP, as sourced from the IMF World Economic Outlook Database. Data for both "biotech patents per total patents" (filed with the Patent Cooperation Treaty) and "business expenditures on biotechnology R&D" came from the Organisation for Economic Co-operation and Development (OECD). And the U.S. National Science Foundation's Science and Engineering Indicators was the source for "Value added of knowledge- and technology-intensive industries."

Last year, Denmark held its long lead in this category, followed by the United States, Australia and Singapore. This year the same three countries took the top three spots. Spain advanced to fourth place, largely due to a surge in the proportion of biotech patent applications filed there.




## SCORECARD CATEGORY #4: EDUCATION/WORKFORCE

***High-tech innovation demands a highly educated workforce***

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 tasks, such as laboratory processes.

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.

## SCORECARD CATEGORY #5: ENTERPRISE SUPPORT

***A trio tussles for the top spot***

No one wants to start a business where there is no endemic support for it. The Scorecard's **Enterprise Support** metric quantifies a country's business-friendly features and the availability of capital in various forms. Consequently, resolving enterprise support problems—to tap an underserved market, to reduce operating costs or to enable new business models—can yield great returns.

The Enterprise Support metric is generated using the average of four elements. The "business-friendly environment" measurement was drawn from *Doing Business 2014* (World Bank and the International Finance Corporation), which surveyed local experts on a synthetic business case—admittedly limited because it relies on 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. World Economic Forum [2014]) 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 in first, followed by the United States and Singapore. This year Singapore leads, trailed by the United States and Hong Kong.

SCORECARD CATEGORY #6:

## FOUNDATIONS

*Finland finishes first*

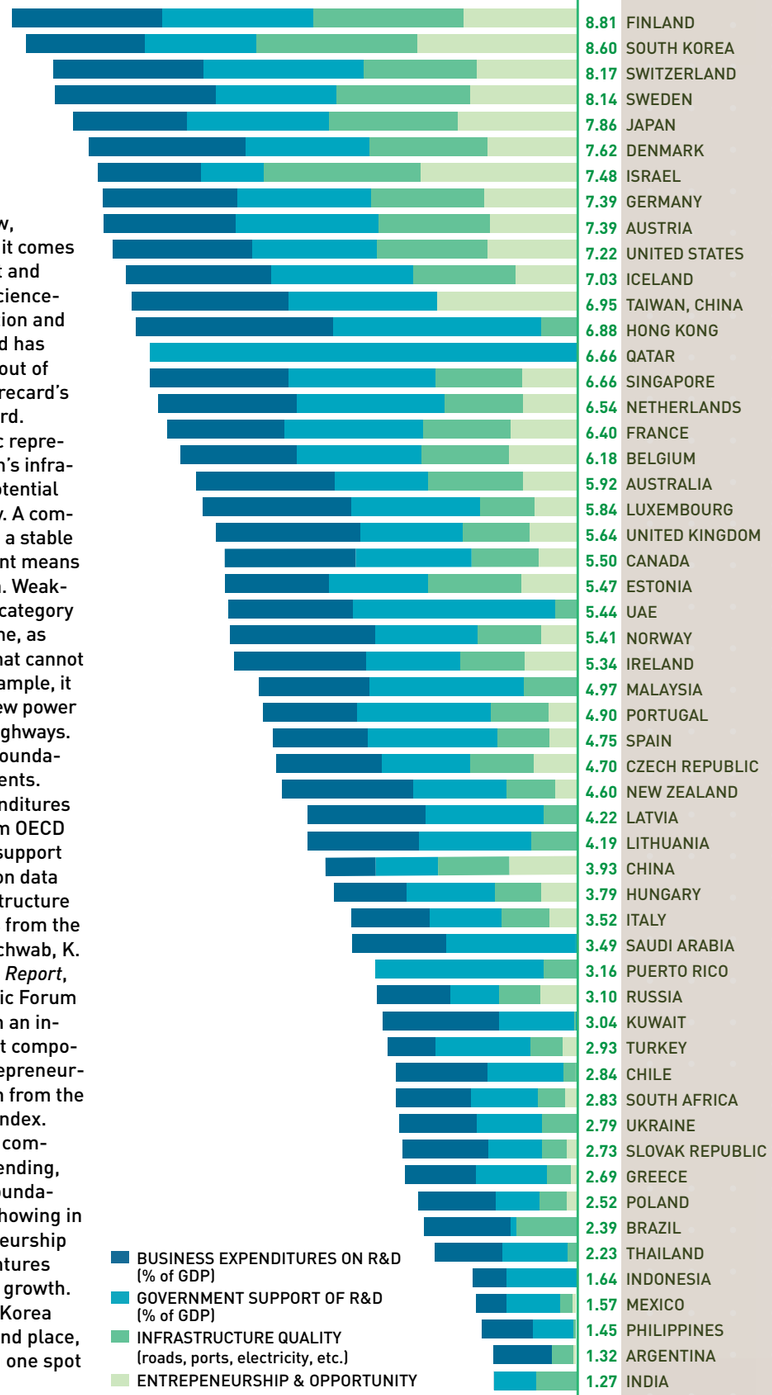
For the fourth year in a row, Finland conquers all when it comes to **Foundations**, those "nut and bolts" factors that allow science-based enterprises to function and flourish. Moreover, Finland has taken the top spot for five out of the seven years of the Scorecard's history. That's quite a record.

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.

To assess a country's Foundations, we use four components. First, "R&D business expenditures per GDP" is generated from OECD figures. For "government support of R&D per GDP," we rely on data from UNESCO. Our "infrastructure quality" component comes from the World Economic Forum (Schwab, K. *The Global Competitiveness Report*, 2014–2015. World Economic Forum (2014))—an index based on an international survey. The last component, "innovation and entrepreneurship opportunity," is drawn from the 2014 Legatum Prosperity Index.

This category includes components based on R&D spending, which can impact future foundations. Likewise, a strong showing in "innovation and entrepreneurship opportunity" may yield ventures that fuel organic domestic growth.

Behind Finland, South Korea climbed from third to second place, pushing Switzerland down one spot in the process.





SCORECARD CATEGORY #7:

## POLICY & STABILITY

*Nordic nations still on top, while the U.S. flounders*

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 slots, respectively. The United States continues to place poorly, finishing 20th.

## COMPONENT SCORES

| | PRODUCTIVITY(1) | | IP(2) | | INTENSITY(3) | | | | | | ENTERPRISE SUPPORT(4) | | | | EDUCATION / WORKFORCE(5) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | a | b | c | d | e | f | g | h | i | j | k | l | m | n | o | p | q | r | s |
| UNITED STATES | 10 | 10 | 10 | 7.63 | 4.4 | 3.33 | 6.91 | 6.25 | 10 | 10 | 8.16 | 10 | 8.66 | 9.17 | 4.44 | 5.35 | | | 10 |
| DENMARK | 0.28 | 0.31 | 9.05 | 7.63 | 7.88 | 10 | 10 | 10 | 0.14 | 0.35 | 8.81 | 0.22 | 2.33 | 8.19 | 4.2 | 2.01 | 8.66 | | 0.28 |
| NEW ZEALAND | | | 6.08 | 9.47 | | | | 7.08 | 0.05 | | 9.6 | | 7 | 6.88 | 10 | 10 | 4.37 | | 0.53 |
| AUSTRALIA | 0.6 | 1.6 | 6.8 | 8.15 | 10 | 4.4 | 4.63 | 6.25 | 0.92 | 0.04 | 7.78 | 0.25 | 5.33 | 8.37 | 7.06 | 5.82 | 5.19 | 3.44 | 3.36 |
| SINGAPORE | | | 6.98 | 10 | | | | 1.25 | 0.12 | | 10 | | 8.33 | 9.26 | | | 5.6 | 6.1 | 0.7 |
| FINLAND | 0 | 0.03 | 9.05 | 10 | 1.03 | 0.04 | 0.18 | 1.87 | 0.08 | 0.03 | 7.83 | 0.07 | 8.33 | 8.26 | 3.6 | 1.95 | 9.03 | | 0.22 |
| SWITZERLAND | 0.23 | 0.31 | 7.52 | 9.47 | 5.44 | 3.05 | 4.15 | 5 | 0.32 | 0.97 | 6.94 | 0.3 | 5.33 | 8.73 | 3.61 | 3.33 | 6.06 | | 0.58 |
| SWEDEN | 0.06 | 0.54 | 8.46 | 8.15 | 7.9 | 1.04 | 1.41 | 2.5 | 0.25 | 0.2 | 7.76 | 0.54 | 8 | 8.41 | 2.46 | 2.31 | 7.26 | | 0.37 |
| UNITED KINGDOM | 0.59 | 0.89 | 8.46 | 9.21 | 1.97 | 0.81 | 2.74 | 5 | 1.36 | | 7.86 | 0.81 | 6 | 9.33 | 7.6 | 6.41 | 5.03 | 3.77 | 5.76 |
| CANADA | 0.02 | 0.97 | 9.05 | 8.68 | 3.93 | 0.29 | 0.18 | 5.83 | 0.84 | 0.12 | 7.32 | 0.95 | 6 | 10 | | 6.41 | 5.37 | 3.96 | 1.62 |
| HONG KONG | 0.07 | 0.03 | 5.18 | 8.94 | 0.54 | 1.31 | 3.16 | | | | 9.03 | | 8.33 | 9.42 | | | 2.78 | | 0.27 |
| GERMANY | 0.11 | 0.5 | 8.28 | 7.89 | 0.87 | 0.33 | 0.35 | 2.23 | 1.57 | 0.43 | 7.51 | 0.63 | 5.33 | 6.85 | 4.83 | 2.94 | 5.94 | 4.51 | 2.78 |
| IRELAND | 0.08 | 0.11 | 9.05 | 8.42 | 3.4 | 3 | 4 | 3.74 | 0.09 | 0.14 | 7.6 | 0.01 | 4 | 7.72 | 7.33 | 4.27 | 5.14 | | 0.13 |
| NETHERLANDS | 0.15 | 0.11 | 9.05 | 8.68 | 0.97 | 1.96 | 2.07 | 4.16 | 0.4 | 0.15 | 6.13 | 0.16 | 5.66 | 8.3 | 2.57 | 0.86 | 5.72 | | 0.76 |
| FRANCE | 0.31 | 0.85 | 9.05 | 8.42 | 1.81 | 1.31 | 1.32 | 4.43 | 1.33 | 1.24 | 5.8 | 0.87 | 5 | 7.19 | 5.31 | 2.96 | 6.36 | 2.96 | 3.65 |
| JAPAN | 0 | 0.11 | 9.05 | 9.47 | 0.12 | 0 | 0 | 1.72 | 2.73 | 0.46 | 6.07 | 0.13 | 5.33 | 6.59 | 0.93 | | 5.81 | 5.06 | 2.02 |
| NORWAY | 0.01 | 0.19 | 6.8 | 8.42 | 5.32 | 0.51 | 0.3 | 3.33 | 0.16 | 0.05 | 8.28 | 0.03 | 8.33 | 7.61 | 2.74 | 1.51 | 6.12 | | 0.23 |
| ISRAEL | 0 | 0.42 | 6.62 | 5.78 | 7.71 | 0.78 | 0.15 | 5.73 | 0.13 | 0.14 | 5.03 | | 8 | 6.45 | | 4.19 | 9.64 | 3.24 | 0.03 |
| AUSTRIA | 0 | 0.03 | 7.52 | 8.15 | 0.66 | 0.15 | 0.15 | 4.16 | 0.13 | 0.05 | 6.83 | 0.04 | 3 | 5.99 | 3.49 | 2.9 | 6.29 | | 0.76 |
| LUXEMBOURG | | | 6.66 | 9.73 | | | | | | | 3.97 | 0 | 8 | | | 0.58 | 10 | | |
| BELGIUM | 0.04 | 0.23 | 9.05 | 7.63 | 3.14 | 1.06 | 1.11 | 6.66 | 0.24 | 0.24 | 4.99 | 0.22 | 5 | 6.83 | 2.6 | 1.57 | 6.1 | | 0.56 |
| QATAR | | | | 9.47 | | | | | 0.01 | | 4.66 | | 10 | | 0 | | | | 0.08 |
| SOUTH KOREA | | | 7.52 | 3.42 | | | | 2.91 | 0.49 | 0.44 | 8.58 | 0.14 | 1.33 | 8.08 | 4.35 | 3.68 | 6.28 | 3.43 | 0.79 |
| ICELAND | | | 3.82 | 6.31 | | | | | | | 7.66 | | 3.33 | | 4.09 | 4.72 | 7.76 | | 0 |
| TAIWAN, CHINA | 0 | 0.03 | 4.86 | 7.1 | 0.23 | 0.01 | 0.01 | 2.5 | 0.19 | | 7.21 | | 7 | 6.19 | | | | 2.32 | |
| ESTONIA | | | | 6.57 | | | | | | 0 | 7.25 | | 5.33 | 6.97 | 4.5 | 2.77 | 3.99 | | 0.01 |
| UAE | | | | 8.15 | | | | | 0.07 | | 6.65 | | 8.66 | 6.7 | | | 0.71 | | 0.72 |
| SPAIN | | | 7.52 | 3.15 | | | | 6.66 | 0.57 | 0.28 | 5.59 | 0.18 | 1.66 | 6.57 | 3.24 | 2.52 | 4.91 | 2.5 | 0.74 |
| MALAYSIA | | | 3.69 | 7.36 | | | | | 0.06 | | 7.24 | | 9.33 | 7.34 | 3.33 | | 1.9 | | 0.84 |
| PORTUGAL | | | 7.74 | 5.78 | | | | | 0.06 | 0.01 | 6.43 | 0 | 2.33 | 6.9 | 3.01 | 4.56 | 5.01 | | 0.23 |
| PUERTO RICO | | | | 9.21 | | | | | | | 4.77 | | 3.66 | | 3.03 | | 1.5 | | |
| CZECH REPUBLIC | | | 7.52 | 3.94 | | | | | 0.04 | 0.05 | 4.95 | 0 | 4.33 | 4.36 | 4.6 | 2.95 | 5.01 | | 0.51 |
| CHILE | | | 7.29 | 3.94 | | | | | 0.07 | | 5.03 | | 5 | 5.79 | 1.85 | 0.34 | 0.53 | 6.52 | 0.03 |
| LITHUANIA | | | 6.03 | 3.68 | | | | | | | 6.51 | | 3 | 4.81 | 3.05 | | 3.24 | | 0.02 |
| SLOVAK REPUBLIC | | | 6.98 | 3.68 | | | | | 0 | 0 | 5.2 | | 3.33 | 4.07 | 4.78 | 4.54 | 3.13 | | 0.1 |
| SOUTH AFRICA | | | 7.16 | 7.63 | | | | 2.5 | 0.09 | 0.02 | 4.98 | | 4.66 | 5.32 | | 0.92 | 0.77 | | 0.94 |
| ITALY | 0 | 0.11 | 9.05 | 3.42 | 0.26 | 0 | 0.04 | 2.82 | 0.79 | 0.14 | 4.23 | 0.04 | 0.66 | 4.89 | 2.04 | 2.78 | 4.22 | 3.17 | 1.03 |
| LATVIA | | | | 4.21 | | | | | | | 6.63 | | 4 | 3.25 | 2.93 | 0.67 | 2.51 | | 0.02 |
| POLAND | 0.01 | 0.03 | 6.98 | 3.42 | 0.13 | 0.19 | 0.27 | 5 | 0.13 | 0.02 | 5.71 | 0 | 1.66 | 2.82 | 5.22 | 3.68 | 2.21 | | 0.3 |
| SAUDI ARABIA | | | 1.44 | 6.57 | | | | | 0.05 | | 4.67 | | 5.33 | 4.76 | 5.04 | 1.67 | | 10 | 0.61 |
| HUNGARY | | | 8.28 | 3.42 | | | | | 0.02 | | 4.32 | 0 | 1 | 4.58 | 1.95 | 0.89 | 3.73 | | 0.22 |
| CHINA | 0.07 | 0.07 | 6.39 | 4.21 | 0 | 0.03 | 0.09 | 1.66 | 2.71 | | 2.51 | | 7 | 4.98 | | | 1.67 | 0.31 | 1.19 |
| GREECE | | | 7.38 | 3.94 | | | | | 0.06 | | 3.71 | 0 | 0.33 | 4.18 | 3.54 | 0.6 | 4.02 | 1.1 | 0.43 |
| MEXICO | | | 5.49 | 2.89 | | | | 4.16 | 0.37 | 0.02 | 5.11 | | 2.33 | 3.87 | 0.96 | 0.96 | 0.58 | 3.05 | |
| TURKEY | | | 6.08 | 3.42 | | | | 0 | 0.26 | | 4.28 | | 2.33 | 2.8 | 3 | 0.97 | 1.52 | 3.24 | 0.5 |
| BRAZIL | | | 4.18 | 2.36 | | | | 5 | 0.73 | | 1.17 | | 2.66 | 3.07 | 1.18 | 0.44 | 1.08 | 5.15 | 0.18 |
| RUSSIA | | | 4.59 | 1.57 | | | | 3.75 | 0.52 | 0.04 | 3.69 | | 3 | 2.67 | 4.32 | 0 | 4.72 | 1.69 | 2.33 |
| THAILAND | | | 0 | 1.84 | | | | | 0.08 | | 6.2 | | 4 | 6.12 | | | 0.55 | 7.25 | |
| KUWAIT | | | | 2.89 | | | | | 0.01 | | 2.66 | | 3 | 5.47 | | | 0.11 | | |
| PHILIPPINES | | | 6.84 | 3.42 | | | | | 0.06 | | 2.36 | | 5 | 1.91 | | | 0 | 2.44 | |
| INDIA | 0.05 | 0.03 | 4.95 | 3.42 | 0 | 0.02 | 0.35 | 4.16 | 0.54 | | 0 | | 5.66 | 4.07 | | | 0.29 | 0 | 0.41 |
| INDONESIA | | | 0.49 | 4.47 | | | | | 0.16 | | 1.51 | | 7 | 1.87 | 0.69 | | | 4.67 | 0.08 |
| UKRAINE | | | 4.59 | 0.78 | | | | | 0.03 | | 2.2 | | 1.66 | 0 | 3.64 | | 2.09 | 0.99 | 0.57 |
| ARGENTINA | | | 5.94 | 0 | | | | | 0.13 | | 1.02 | | 0 | 0.17 | 1.55 | 0.42 | 1.59 | 4.67 | |

| | FOUNDATIONS(6) | | | | POLICY & STABILITY(7) | | | |
|---|---|---|---|---|---|---|---|---|
| | t | u | v | w | x | y | z | aa |
| UNITED STATES | 5.59 | 6.85 | 7.77 | 8.66 | 6.96 | 7.63 | 7.61 | 8.45 |
| DENMARK | 5.62 | 7.32 | 7.77 | 9.77 | 8.18 | 9.3 | 9.46 | 9.66 |
| NEW ZEALAND | 1.39 | 3.02 | 5.83 | 8.15 | 10 | 8.5 | 9.5 | 9.61 |
| AUSTRALIA | 3.4 | 5.84 | 5.83 | 8.59 | 8.43 | 8.07 | 9.42 | 9.23 |
| SINGAPORE | 3.43 | 5.44 | 9.16 | 8.61 | 9.58 | 9.66 | 10 | 9.19 |
| FINLAND | 7.08 | 9.39 | 9.44 | 9.34 | 9.67 | 10 | 9.62 | 9.84 |
| SWITZERLAND | 6.26 | 7.05 | 10 | 9.37 | 9.72 | 8.71 | 8.89 | 9.36 |
| SWEDEN | 6.68 | 8.36 | 7.5 | 10 | 8.83 | 9.01 | 9.76 | 9.95 |
| UNITED KINGDOM | 3 | 4.15 | 6.38 | 9.02 | 6.51 | 7.52 | 9.34 | 8.94 |
| CANADA | 2.43 | 4.18 | 7.22 | 8.17 | 8.48 | 8.59 | 9.16 | 9.18 |
| HONG KONG | | 1.71 | 9.72 | 9.2 | 7.95 | 8.45 | 9.88 | 8.47 |
| GERMANY | 5.8 | 7.1 | 8.33 | 8.34 | 8.11 | 7.69 | 8.61 | 8.73 |
| IRELAND | 3.31 | 4 | 5.83 | 8.23 | 7.93 | 7.5 | 8.7 | 9.11 |
| NETHERLANDS | 3.37 | 4.93 | 9.16 | 8.68 | 8.8 | 8.57 | 9.34 | 9.43 |
| FRANCE | 4.16 | 5.49 | 8.61 | 7.35 | 6.29 | 7.52 | 7.24 | 7.96 |
| JAPAN | 7.47 | 8.01 | 8.88 | 7.08 | 8.31 | 7.96 | 7.09 | 8 |
| NORWAY | 2.27 | 3.97 | 6.38 | 9.02 | 9.57 | 8.92 | 8.96 | 10 |
| ISRAEL | 9.75 | 9.82 | 3.88 | 6.45 | 0.82 | 6.62 | 7.26 | 6.36 |
| AUSTRIA | 5.44 | 6.97 | 8.88 | 8.25 | 9.61 | 7.86 | 8.36 | 9.5 |
| LUXEMBOURG | 2.7 | 3.37 | 8.05 | 9.24 | 9.57 | 8.03 | 9.32 | 9.35 |
| BELGIUM | 4.28 | 5.46 | 7.77 | 7.21 | 8.07 | 7.94 | 7.73 | 7.97 |
| QATAR | | | 6.66 | | 9.16 | 6.1 | 5.86 | 6.69 |
| SOUTH KOREA | 10 | 10 | 6.94 | 7.45 | 5.62 | 6.28 | 6.68 | 6.31 |
| ICELAND | 3.86 | 6.37 | 8.88 | 9.01 | 9.31 | 7.56 | 7.05 | 8.84 |
| TAIWAN, CHINA | 6.56 | | 6.94 | 7.36 | 7.88 | 6.53 | 7.21 | 6.69 |
| ESTONIA | 3.49 | 5.79 | 6.11 | 6.5 | 7.38 | 5.79 | 8.19 | 7.12 |
| UAE | | 1.05 | 9.44 | 5.83 | 8.08 | 6.44 | 5.99 | 5.25 |
| SPAIN | 1.76 | 3.24 | 8.05 | 5.96 | 4.82 | 6.37 | 6.5 | 6.52 |
| MALAYSIA | | 2.51 | 7.22 | 5.18 | 4.95 | 6.21 | 5.44 | 4.65 |
| PORTUGAL | 1.79 | 3.65 | 8.33 | 5.84 | 7.44 | 6.66 | 6.02 | 6.65 |
| PUERTO RICO | | 1.05 | 5.27 | | 5.69 | 3.59 | 6.21 | 5.38 |
| CZECH REPUBLIC | 2.73 | 3.95 | 5.55 | 6.58 | 8.56 | 5.41 | 7.04 | 6.54 |
| CHILE | 0 | 0.88 | 4.72 | 5.77 | 6.11 | 6.72 | 8.37 | 7.74 |
| LITHUANIA | | 2.14 | 5.27 | 5.17 | 8.09 | 5.23 | 7.18 | 5.78 |
| SLOVAK REPUBLIC | 0.69 | 1.53 | 3.33 | 5.37 | 8.73 | 5.06 | 6.45 | 4.55 |
| SOUTH AFRICA | 0.75 | 1.73 | 4.16 | 4.67 | 4.56 | 3.84 | 4.73 | 3.4 |
| ITALY | 1.76 | 2.97 | 4.44 | 4.89 | 6.6 | 3.9 | 5.96 | 4.23 |
| LATVIA | | 1.58 | 5.55 | 5.54 | 6.83 | 5.43 | 6.83 | 5.62 |
| POLAND | 0.66 | 1.73 | 2.77 | 4.93 | 8.18 | 4.81 | 6.9 | 5.76 |
| SAUDI ARABIA | | 0 | 6.11 | 4.36 | 3.29 | 2.52 | 3.61 | 3.9 |
| HUNGARY | 2.24 | 2.89 | 5.55 | 4.49 | 7.58 | 4.59 | 6.36 | 4.97 |
| CHINA | 4.25 | 4.45 | 3.88 | 3.13 | 2.79 | 2.2 | 2.31 | 1.32 |
| GREECE | 0.39 | 1.51 | 4.44 | 4.41 | 4.05 | 3.89 | 5.44 | 4.52 |
| MEXICO | 0.18 | 0.9 | 3.33 | 1.87 | 2.1 | 3.39 | 4.9 | 0.88 |
| TURKEY | 0.94 | 1.98 | 5.83 | 2.98 | 0.45 | 3.61 | 4.79 | 3.23 |
| BRAZIL | | 2.87 | 0.27 | 4.04 | 3.76 | 2.02 | 3.57 | 2.52 |
| RUSSIA | 2.27 | 2.56 | 3.05 | 4.5 | 2.06 | 1.02 | 2.1 | 0.14 |
| THAILAND | | 0.45 | 3.05 | 3.18 | 0 | 3.06 | 4.07 | 2.47 |
| KUWAIT | | 0.05 | 3.61 | 5.47 | 5.28 | 2.04 | 3.06 | 4.34 |
| PHILIPPINES | | 0.1 | 1.94 | 2.3 | 0.94 | 2.51 | 3.11 | 1.42 |
| INDIA | | 1.86 | 1.94 | 0 | 0.48 | 1.63 | 1.74 | 2.6 |
| INDONESIA | | 0.02 | 3.33 | 1.58 | 2.96 | 1.46 | 2.68 | 0.96 |
| UKRAINE | | 1.68 | 3.05 | 3.64 | 2.03 | 0 | 1.18 | 0 |
| ARGENTINA | 0.15 | 1.46 | 0 | 3.65 | 4.98 | 1.27 | 0 | 0.33 |

## OVERALL CATEGORY SCORES

| | (1) | (2) | (3) | (4) | (5) | (6) | (7) | SCORE | | RANK |
|---|---|---|---|---|---|---|---|---|---|---|
| UNITED STATES | 10.00 | 8.82 | 6.18 | 9.00 | 6.60 | 7.22 | 7.66 | 39.62 | UNITED STATES | 1 |
| DENMARK | 0.30 | 8.34 | 7.60 | 4.89 | 3.79 | 7.62 | 9.15 | 29.77 | DENMARK | 2 |
| NEW ZEALAND | | 7.78 | 3.57 | 7.83 | 6.23 | 4.60 | 9.40 | 28.14 | NEW ZEALAND | 3 |
| AUSTRALIA | 1.10 | 7.48 | 5.24 | 5.43 | 4.97 | 5.92 | 8.79 | 27.80 | AUSTRALIA | 4 |
| SINGAPORE | | 8.49 | 0.69 | 9.20 | 4.13 | 6.66 | 9.61 | 27.69 | SINGAPORE | 5 |
| FINLAND | 0.02 | 9.53 | 0.64 | 6.12 | 3.70 | 8.81 | 9.78 | 27.57 | FINLAND | 6 |
| SWITZERLAND | 0.27 | 8.50 | 3.59 | 5.33 | 3.40 | 8.17 | 9.17 | 27.44 | SWITZERLAND | 7 |
| SWEDEN | 0.30 | 8.31 | 2.62 | 6.18 | 3.10 | 8.14 | 9.39 | 27.16 | SWEDEN | 8 |
| UNITED KINGDOM | 0.74 | 8.84 | 2.38 | 6.00 | 5.71 | 5.64 | 8.08 | 26.70 | UNITED KINGDOM | 9 |
| CANADA | 0.50 | 8.87 | 2.21 | 6.07 | 4.34 | 5.50 | 8.85 | 25.95 | CANADA | 10 |
| HONG KONG | 0.05 | 7.06 | 1.67 | 8.93 | 1.53 | 6.88 | 8.69 | 24.85 | HONG KONG | 11 |
| GERMANY | 0.31 | 8.09 | 1.07 | 5.08 | 4.20 | 7.39 | 8.29 | 24.58 | GERMANY | 12 |
| IRELAND | 0.10 | 8.74 | 2.85 | 4.83 | 4.22 | 5.34 | 8.31 | 24.56 | IRELAND | 13 |
| NETHERLANDS | 0.13 | 8.87 | 1.91 | 5.06 | 2.48 | 6.54 | 9.04 | 24.30 | NETHERLANDS | 14 |
| FRANCE | 0.58 | 8.74 | 2.04 | 4.72 | 4.25 | 6.40 | 7.25 | 24.27 | FRANCE | 15 |
| JAPAN | 0.06 | 9.26 | 0.91 | 4.53 | 3.46 | 7.86 | 7.84 | 24.22 | JAPAN | 16 |
| NORWAY | 0.10 | 7.61 | 1.92 | 6.06 | 2.65 | 5.41 | 9.36 | 23.66 | NORWAY | 17 |
| ISRAEL | 0.21 | 6.20 | 2.90 | 6.49 | 4.28 | 7.48 | 5.27 | 23.44 | ISRAEL | 18 |
| AUSTRIA | 0.02 | 7.84 | 1.05 | 3.97 | 3.36 | 7.39 | 8.83 | 23.17 | AUSTRIA | 19 |
| LUXEMBOURG | | 8.20 | | 3.99 | 5.29 | 5.84 | 9.07 | 23.13 | LUXEMBOURG | 20 |
| BELGIUM | 0.14 | 8.34 | 2.44 | 4.26 | 2.71 | 6.18 | 7.93 | 22.85 | BELGIUM | 21 |
| QATAR | | 9.47 | 0.01 | 7.33 | 0.04 | 6.66 | 6.95 | 21.76 | QATAR | 22 |
| SOUTH KOREA | | 5.47 | 1.70 | 4.53 | 3.71 | 8.60 | 6.22 | 21.59 | SOUTH KOREA | 23 |
| ICELAND | | 5.07 | | 5.50 | 4.14 | 7.03 | 8.19 | 21.37 | ICELAND | 24 |
| TAIWAN, CHINA | 0.02 | 5.98 | 0.59 | 6.80 | 2.32 | 6.95 | 7.08 | 21.24 | TAIWAN, CHINA | 25 |
| ESTONIA | | 6.57 | | 6.52 | 2.82 | 5.47 | 7.12 | 20.35 | ESTONIA | 26 |
| UAE | | 8.15 | 0.07 | 7.34 | 0.72 | 5.44 | 6.44 | 20.11 | UAE | 27 |
| SPAIN | | 5.34 | 3.62 | 3.50 | 2.78 | 4.75 | 6.05 | 18.60 | SPAIN | 28 |
| MALAYSIA | | 5.53 | 0.06 | 7.97 | 2.02 | 4.97 | 5.31 | 18.47 | MALAYSIA | 29 |
| PORTUGAL | | 6.76 | 0.06 | 3.92 | 3.20 | 4.90 | 6.69 | 18.24 | PORTUGAL | 30 |
| PUERTO RICO | | 9.21 | | 4.22 | 2.27 | 3.16 | 5.22 | 17.19 | PUERTO RICO | 31 |
| CZECH REPUBLIC | | 5.73 | 0.04 | 3.41 | 3.27 | 4.70 | 6.89 | 17.17 | CZECH REPUBLIC | 32 |
| CHILE | | 5.62 | 0.07 | 5.27 | 1.85 | 2.84 | 7.24 | 16.35 | CHILE | 33 |
| LITHUANIA | | 4.86 | | 4.77 | 2.10 | 4.19 | 6.57 | 16.07 | LITHUANIA | 34 |
| SLOVAK REPUBLIC | | 5.33 | 0.00 | 4.20 | 3.14 | 2.73 | 6.20 | 15.43 | SLOVAK REPUBLIC | 35 |
| SOUTH AFRICA | | 7.40 | 1.30 | 4.99 | 0.88 | 2.83 | 4.13 | 15.37 | SOUTH AFRICA | 36 |
| ITALY | 0.06 | 6.24 | 0.78 | 2.46 | 2.65 | 3.52 | 5.17 | 14.90 | ITALY | 37 |
| LATVIA | | 4.21 | | 4.63 | 1.53 | 4.22 | 6.18 | 14.84 | LATVIA | 38 |
| POLAND | 0.02 | 5.20 | 1.14 | 2.55 | 2.85 | 2.52 | 6.41 | 14.79 | POLAND | 39 |
| SAUDI ARABIA | | 4.01 | 0.05 | 4.92 | 4.33 | 3.49 | 3.33 | 14.38 | SAUDI ARABIA | 40 |
| HUNGARY | | 5.85 | 0.02 | 2.48 | 1.70 | 3.79 | 5.88 | 14.08 | HUNGARY | 41 |
| CHINA | 0.07 | 5.30 | 0.90 | 4.83 | 1.06 | 3.93 | 2.16 | 13.03 | CHINA | 42 |
| GREECE | | 5.66 | 0.06 | 2.06 | 1.94 | 2.69 | 4.48 | 12.05 | GREECE | 43 |
| MEXICO | | 4.19 | 2.27 | 3.77 | 1.39 | 1.57 | 2.82 | 11.43 | MEXICO | 44 |
| TURKEY | | 4.75 | 0.13 | 3.14 | 1.85 | 2.93 | 3.02 | 11.30 | TURKEY | 45 |
| BRAZIL | | 3.27 | 2.87 | 2.30 | 1.61 | 2.39 | 2.97 | 11.00 | BRAZIL | 46 |
| RUSSIA | | 3.08 | 2.14 | 3.12 | 2.61 | 3.10 | 1.33 | 10.98 | RUSSIA | 47 |
| THAILAND | | 0.92 | 0.08 | 5.44 | 3.90 | 2.23 | 2.40 | 10.69 | THAILAND | 48 |
| KUWAIT | | 2.89 | 0.01 | 3.71 | 0.11 | 3.04 | 3.68 | 9.60 | KUWAIT | 49 |
| PHILIPPINES | | 5.13 | 0.06 | 3.09 | 1.22 | 1.45 | 2.00 | 9.24 | PHILIPPINES | 50 |
| INDIA | 0.04 | 4.19 | 1.01 | 3.24 | 0.23 | 1.27 | 1.61 | 8.28 | INDIA | 51 |
| INDONESIA | | 2.48 | 0.16 | 3.46 | 1.81 | 1.64 | 2.02 | 8.27 | INDONESIA | 52 |
| UKRAINE | | 2.69 | 0.03 | 1.29 | 1.82 | 2.79 | 0.80 | 6.73 | UKRAINE | 53 |
| ARGENTINA | | 2.97 | 0.13 | 0.40 | 2.06 | 1.32 | 1.65 | 6.08 | ARGENTINA | 54 |

**(A)** PUBLIC COMPANY REVENUES (US$MM)
**(B)** PUBLIC COMPANIES
(C) PATENT STRENGTH
(D) PERCEIVED IP PROTECTION
(E) PUBLIC COMPANIES/ MILLION POPULATION
(F) PUBLIC COMPANY EMPLOYEES/ CAPITA
(G) PUBLIC COMPANY REVENUES/ $USB GDP
(H) BIOTECH PATENTS/ TOTAL PATENTS FILED WITH PCT
(I) VALUE ADDED OF KNOWLEDGE- AND TECHNOLOGY-INTENSIVE INDUSTRIES
(J) BUSINESS EXPENDITURES ON BIOTECHNOLOGY R&D
(K) BUSINESS-FRIENDLY ENVIRONMENT (HIGHER = BETTER)
(L) BIOTECH VC, 2007 (US$MM)
(M) VC AVAILABILITY
(N) CAPITAL AVAILABILITY
(O) POST-SECONDARY SCIENCE GRADUATES/ CAPITA
(P) PHD GRADUATES IN LIFE SCIENCES PER MILLION POPULATION
(Q) R&D PERSONNEL PER THOUSAND EMPLOYMENT
(R) TALENT RETENTION (RECIPROCAL OF BRAIN DRAIN)
(S) BRAIN GAIN (share of global students studying outside their country)
(T) BUSINESS EXPENDITURES ON R&D (% of GDP)
(U) GOVERNMENT SUPPORT OF R&D (% of GDP)
(V) INFRASTRUCTURE QUALITY (roads, ports, electricity, etc.)
(W) ENTREPENEURSHIP & OPPORTUNITY
(X) POLITICAL STABILITY & ABSENCE OF VIOLENCE/ TERRORISM
(Y) GOVERNMENT EFFECTIVENESS
(Z) REGULATORY QUALITY
(AA) RULE OF LAW

# 2015 *SCIENTIFIC AMERICAN WORLDVIEW* OVERALL SCORES

***A growing lead for the United States, with fierce competition among the followers***

Our 2015 Scorecard ranks the biotechnology 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 average 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 subscore 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 scores between the second and 20th-place holder, Luxembourg.

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 Singapore performs poorly in the Intensity category. Conversely, 40th-place Saudi Arabia ranks relatively well in Education/Workplace.

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 to support systems including everything from the availability of capital to the access to ports.

## *SCIENTIFIC AMERICAN WORLDVIEW* SCORECARD METHODOLOGY

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.

| PRODUCTIVITY | |
|---|---|
| public company revenues | Lawrence, S. & Lähteenmäki, *R. Nat. Biotechnol.* **32**, 626–632 (2014), and company disclosures |
| number of public companies | Lawrence, S. & Lähteenmäki, *R. Nat. Biotechnol.* **32**, 626–632 (2014), and company disclosures |

| IP PROTECTION | |
|---|---|
| IP strength | Park, W.G. *Research Policy* **37**, 761–766 (2008) |
| perceived IP protection | Schwab, K. *The Global Competitiveness Report*, 2014–2015. World Economic Forum (2014) |

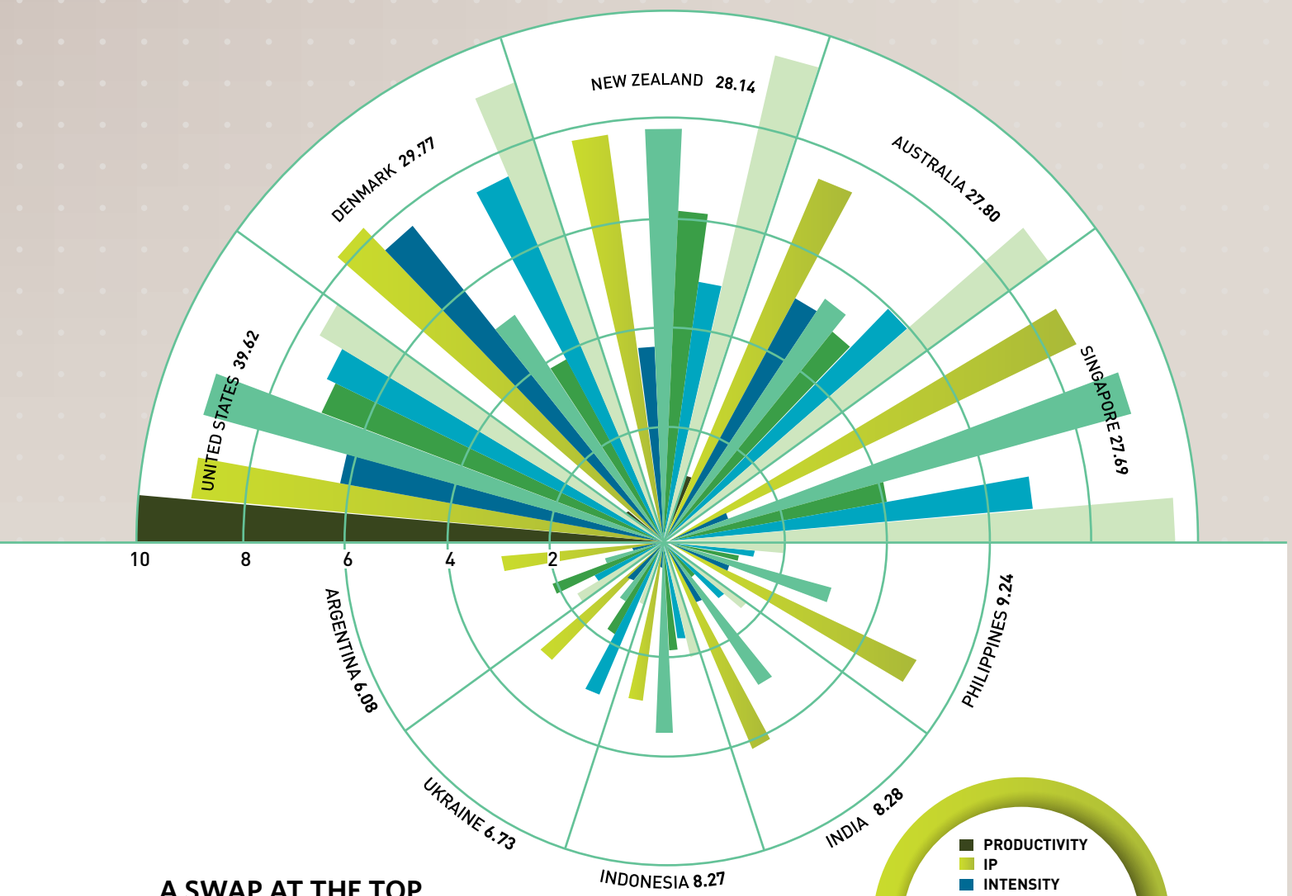
| INTENSITY | |
|---|---|
| public companies per million population | Lawrence, S. & Lähteenmäki, *R. Nat. Biotechnol.* **32**, 626–632 (2014), company disclosures and U.S. Census Bureau International Database |
| public biotechnology company employees per capita | Lawrence, S. & Lähteenmäki, *R. Nat. Biotechnol.* **32**, 626–632 (2014), company disclosures and U.S. Census Bureau International Database |
| public biotechnology company revenues per GDP | Lawrence, S. & Lähteenmäki, *R. Nat. Biotechnol.* **32**, 626–632 (2014), company disclosures and IMF World Economic Outlook Database |
| biotech patents per total patents | Organisation for Economic Co-operation and Development |
| business expenditures on biotechnology R&D | Organisation for Economic Co-operation and Development |
| value added of knowledge- and technology-intensive industries | U.S. National Science Foundation's Science and Engineering Indicator |

| ENTERPRISE SUPPORT | |
|---|---|
| business-friendly environment | Doing Business 2014 (World Bank and the International Finance Corporation) |
| biotechnology venture capital | Organisation for Economic Co-operation and Development |
| venture capital availability | Schwab, K. *The Global Competitiveness Report*, 2014–2015. World Economic Forum (2014) |
| capital availability | Milken Institute Capital Access Index |

| EDUCATION/WORKFORCE | |
|---|---|
| Post-secondary science graduates per capita | UNESCO and U.S. Census Bureau International Database |
| Ph.D. graduates in the life sciences per capita | Organisation for Economic Co-operation and Development |
| R&D personnel per thousand employment | Organisation for Economic Co-operation and Development |
| talent retention | U.S. National Science Foundation |
| brain drain | U.S. National Science Foundation |

| FOUNDATIONS | |
|---|---|
| R&D business expenditures per GDP | Organisation for Economic Co-operation and Development |
| government support of R&D per GDP | UNESCO |
| infrastructure quality | Schwab, K. *The Global Competitiveness Report*, 2014–2015. World Economic Forum (2014) |
| innovation & entrepreneurship opportunity | 2014 Legatum Prosperity Index |

| POLICY & STABILITY | |
|---|---|
| political stability & absence of violence/ terrorism | World Bank's 2014 World Governance Indicators |
| government effectiveness | World Bank's 2014 World Governance Indicators |
| regulatory quality | World Bank's 2014 World Governance Indicators |
| rule of law | World Bank's 2014 World Governance Indicators |




## A SWAP AT THE TOP

***A familiar crew dominates the Top Five***

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 has been the front-runner since the *Scientific American Worldview* Scorecard launched 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 in 2014 to fifth this year. Australia held its ground in fourth this year and last.

## 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 from the bottom 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.

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



## SEVEN YEARS OF BIOTECH TRACKING BY RANK

***Our growing database reveals ongoing competition at many levels***

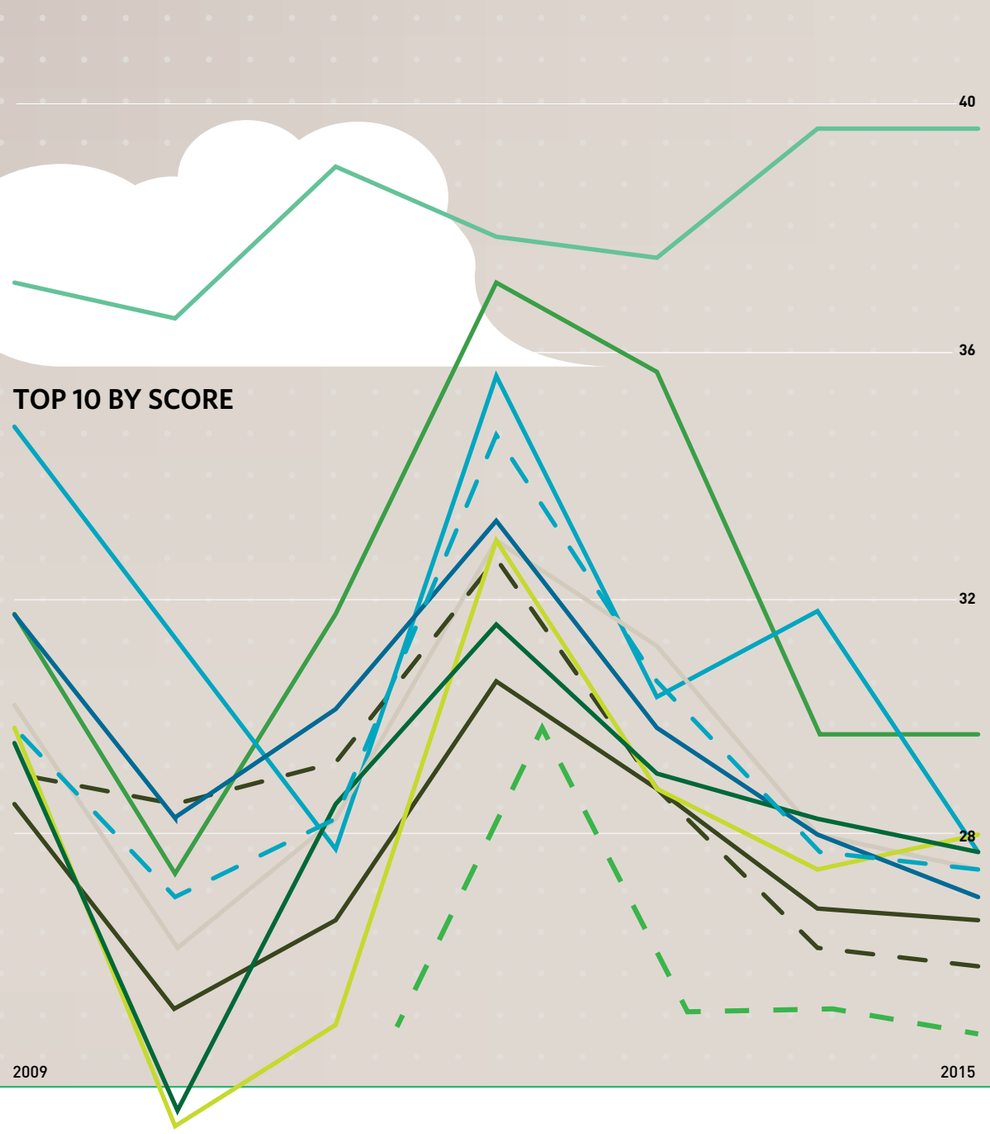
Analyzing the Scorecard data from year to year uncovers certain trends, such as movement or stasis in the Top and Bottom Five, but a longer perspective shows much more. The end results demonstrate how each country changed relative to itself and others. Likewise, these data show the expanding list of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

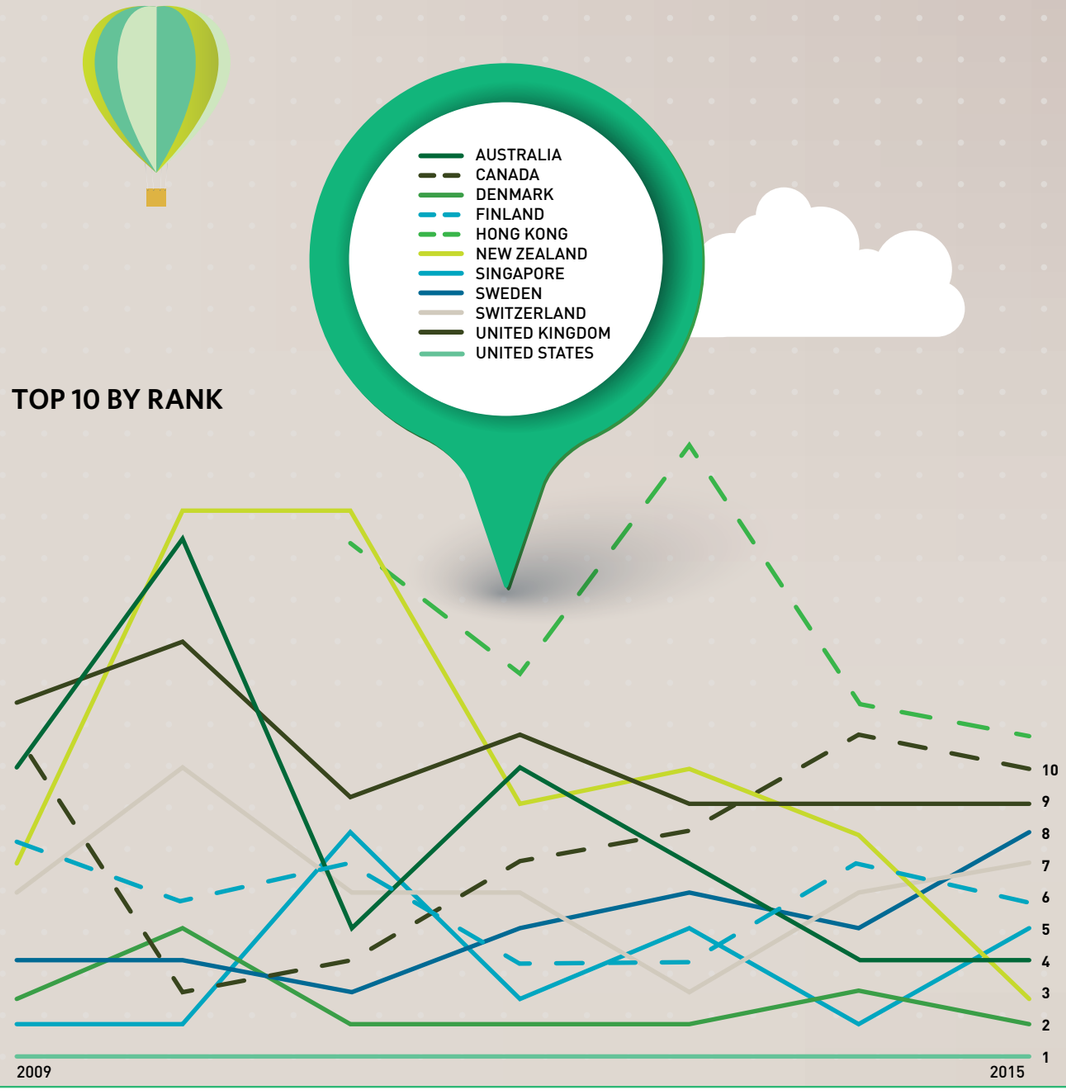
Despite the fact that the United States has maintained its top spot throughout, it is still interesting to observe the dynamics of the other highest-ranked countries. In early years, for example, New Zealand did not crack the Top 10, but in 2012 it ranked 9th and has stayed in the Top 10 ever since—breaking 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, maintained a Top 10 ranking from 2010 through 2013, came in 11th last year, and is in 10th place 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.

change since last year (neg. values = improvement)

| COUNTRY | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | AVG. | |
|---|---|---|---|---|---|---|---|---|---|
| UNITED STATES | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1.0 | 0 |
| DENMARK | 3 | 5 | 2 | 2 | 2 | 3 | 2 | 2.7 | -1 |
| NEW ZEALAND | 7 | 18 | 18 | 9 | 10 | 8 | 3 | 10.4 | -5 |
| AUSTRALIA | 10 | 17 | 5 | 10 | 7 | 4 | 4 | 8.1 | 0 |
| SINGAPORE | 2 | 2 | 8 | 3 | 5 | 2 | 5 | 3.9 | 3 |
| FINLAND | 8 | 6 | 7 | 4 | 4 | 7 | 6 | 6.0 | -1 |
| SWITZERLAND | 6 | 10 | 6 | 6 | 3 | 6 | 7 | 6.3 | 1 |
| SWEDEN | 4 | 4 | 3 | 5 | 6 | 5 | 8 | 5.0 | 3 |
| UNITED KINGDOM | 12 | 14 | 9 | 11 | 9 | 9 | 9 | 10.4 | 0 |
| CANADA | 11 | 3 | 4 | 7 | 8 | 11 | 10 | 7.7 | -1 |
| HONG KONG | | | 17 | 13 | 20 | 12 | 11 | 14.6 | -1 |
| GERMANY | 16 | 16 | 16 | 16 | 14 | 13 | 12 | 14.7 | -1 |
| IRELAND | 14 | 13 | 14 | 8 | 11 | 16 | 13 | 12.7 | -3 |
| NETHERLANDS | 19 | 12 | 12 | 17 | 12 | 14 | 14 | 14.3 | 0 |
| FRANCE | 18 | 8 | 10 | 12 | 13 | 15 | 15 | 13.0 | 0 |
| JAPAN | 13 | 9 | 11 | 18 | 18 | 18 | 16 | 14.7 | -2 |
| NORWAY | 17 | 21 | 21 | 19 | 22 | 19 | 17 | 19.4 | -2 |
| ISRAEL | 5 | 7 | 13 | 14 | 15 | 22 | 18 | 13.4 | -4 |
| AUSTRIA | 21 | 20 | 20 | 20 | 17 | 20 | 19 | 19.6 | -1 |
| LUXEMBOURG | | 25 | 29 | 25 | 19 | 10 | 20 | 21.3 | 10 |
| BELGIUM | 20 | 15 | 15 | 15 | 16 | 21 | 21 | 17.6 | 0 |
| QATAR | | | | | 42 | 25 | 22 | 29.7 | -3 |
| SOUTH KOREA | 15 | 19 | 19 | 22 | 24 | 23 | 23 | 20.7 | 0 |
| ICELAND | 9 | 11 | 22 | 23 | 23 | 24 | 24 | 19.4 | 0 |
| TAIWAN, CHINA | | | | 21 | 26 | 17 | 25 | 22.3 | 8 |
| ESTONIA | | | 27 | 24 | 38 | 26 | 26 | 28.2 | 0 |
| UAE | | | | | 40 | 27 | 27 | 31.3 | 0 |
| SPAIN | 30 | 23 | 23 | 26 | 21 | 28 | 28 | 25.6 | 0 |
| MALAYSIA | | | 28 | 29 | 37 | 29 | 29 | 30.4 | 0 |
| PORTUGAL | 27 | 24 | 24 | 27 | 29 | 31 | 30 | 27.4 | -1 |
| PUERTO RICO | | | | | 52 | 30 | 31 | 37.7 | 1 |
| CZECH REPUBLIC | 23 | 29 | 32 | 30 | 25 | 34 | 32 | 29.3 | -2 |
| CHILE | | | 26 | 32 | 28 | 35 | 33 | 30.8 | -2 |
| LITHUANIA | | | 35 | 33 | 34 | 32 | 34 | 33.6 | 2 |
| SLOVAK REPUBLIC | 34 | 22 | 34 | 28 | 31 | 40 | 35 | 32.0 | -5 |
| SOUTH AFRICA | 24 | 28 | 36 | 37 | 30 | 36 | 36 | 32.4 | 0 |
| ITALY | 26 | 27 | 33 | 36 | 33 | 37 | 37 | 32.7 | 0 |
| LATVIA | | | | 44 | 50 | 38 | 38 | 42.5 | 0 |
| POLAND | 29 | 32 | 38 | 34 | 32 | 39 | 39 | 34.7 | 0 |
| SAUDI ARABIA | | | 25 | 35 | 45 | 33 | 40 | 35.6 | 7 |
| HUNGARY | 28 | 26 | 31 | 31 | 27 | 41 | 41 | 32.1 | 0 |
| CHINA | 25 | 31 | 30 | 43 | 39 | 42 | 42 | 36.0 | 0 |
| GREECE | 36 | 30 | 37 | 38 | 35 | 44 | 43 | 37.6 | -1 |
| MEXICO | 33 | 33 | 41 | 41 | 43 | 46 | 44 | 40.1 | -2 |
| TURKEY | 30 | 34 | 39 | 42 | 44 | 47 | 45 | 40.1 | -2 |
| BRAZIL | 32 | 35 | 42 | 39 | 36 | 45 | 46 | 39.3 | 1 |
| RUSSIA | 22 | 36 | 43 | 45 | 41 | 48 | 47 | 40.3 | -1 |
| THAILAND | | | 40 | 40 | 54 | 43 | 48 | 45.0 | 5 |
| KUWAIT | | | | | 53 | 49 | 49 | 50.3 | 0 |
| PHILIPPINES | | 38 | 45 | 48 | 51 | 51 | 50 | 47.2 | -1 |
| INDIA | 35 | 37 | 44 | 47 | 47 | 52 | 51 | 44.7 | -1 |
| INDONESIA | | | 47 | 50 | 49 | 50 | 52 | 49.6 | 2 |
| UKRAINE | | | 48 | 49 | 48 | 53 | 53 | 50.2 | 0 |
| ARGENTINA | | | 46 | 46 | 46 | 54 | 54 | 49.2 | 0 |




## 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, 38.0, 37.6, 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 31.6, 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.

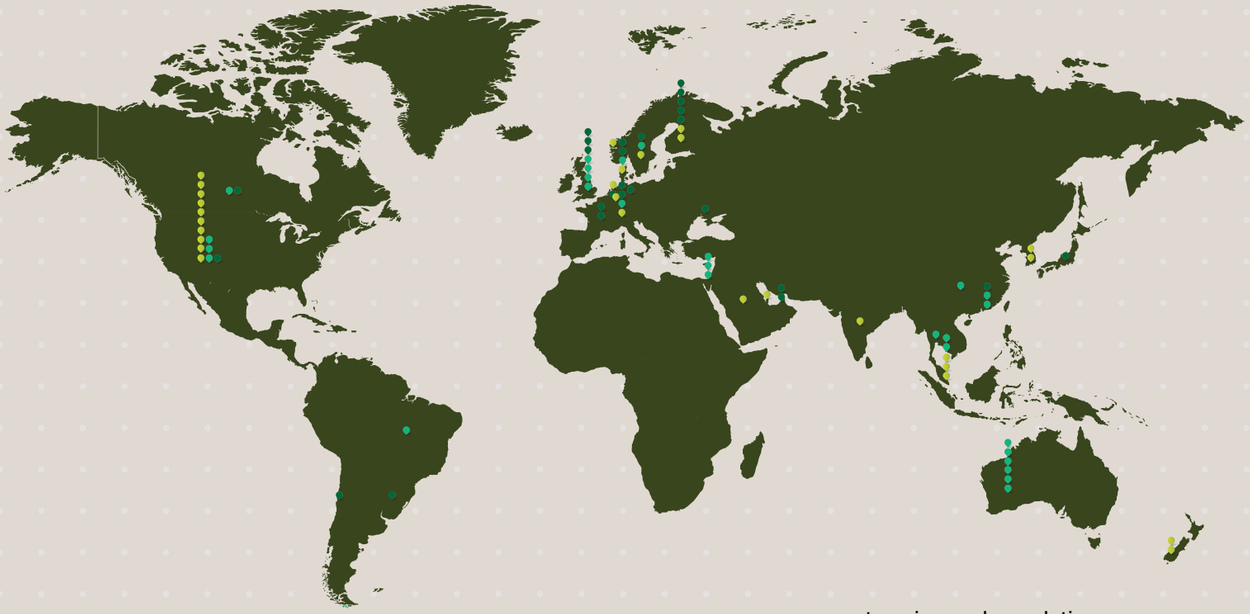
## LESS ROCKING IN THE RANKING

***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.



Countries around the world excel

## 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 venture capital availability." And in some categories, such as relative ones, size doesn't even matter. For instance, Luxembourg—smaller than Rhode Island, and with a population of only about half a million—won "most 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."


**GREATEST PUBLIC COMPANY REVENUES:** United States, Australia, United Kingdom

**MOST PUBLIC COMPANIES:** United States, Australia, Canada

**GREATEST PUBLIC COMPANY MARKET CAPITALIZATION:** United States, Australia, United Kingdom

**MOST PUBLIC COMPANY EMPLOYEES:** United States, Australia, France

**GREATEST REVENUE PER PUBLIC COMPANY:** Netherlands, United States, Denmark

**GREATEST REVENUE PER PUBLIC COMPANY EMPLOYEE:** Finland, United Kingdom, Switzerland/United States

**STRONGEST MEASURED PATENT PROTECTION:** United States

**GREATEST PERCEIVED PATENT STRENGTH:** Finland/Singapore

**GREATEST PERCENTAGE OF PATENTS IN BIOTECHNOLOGY:** Denmark, Singapore, Belgium

**GREATEST ENTERPRISE SUPPORT:** Singapore, United States, Hong Kong

**GREATEST VENTURE CAPITAL AVAILABILITY:** Qatar, United States/United Arab Emirates

**MOST PH.D. GRADUATES IN LIFE SCIENCES PER CAPITA:** New Zealand, Canada/United Kingdom

**MOST PH.D. GRADUATES IN THE LIFE SCIENCES:** United States, United Kingdom, Germany

**MOST R&D PERSONNEL PER TOTAL EMPLOYMENT:** Luxembourg, Israel, Finland

**BEST TALENT RETENTION** *(most U.S.-trained doctorate graduates intending to return home)*: Saudi Arabia, Thailand, Chile

**WORST BRAIN DRAIN** *(most U.S.-trained doctorate graduates intending to stay in the United States):* India, China, Ukraine

**BEST BRAIN GAIN** *(share of global graduate students):* United States, United Kingdom, France

**GREATEST BUSINESS EXPENDITURES ON R&D** *(% of GDP):* South Korea, Israel, Japan

**GOVERNMENT SUPPORT OF R&D** *(% of GDP):* South Korea, Israel, Finland

**BEST INFRASTRUCTURE QUALITY:** Switzerland, Hong Kong, United Arab Emirates/Finland

**STRONGEST PERCEIVED ENTREPRENEURSHIP CLIMATE:** Sweden, Denmark, Switzerland

**BEST POLITICAL STABILITY:** New Zealand, Switzerland, Finland

**GREATEST GOVERNMENT EFFECTIVENESS:** Finland, Singapore, Denmark

**GREATEST REGULATORY QUALITY:** Singapore, Hong Kong, Sweden

**BEST RULE OF LAW:** Norway, Sweden, Finland

**LARGEST PUBLIC MARKETS FOR BIOTECHNOLOGY:** United States, Australia, United Kingdom

**BEST GROWTH IN BIOTECHNOLOGY PUBLIC MARKETS:** United States, Australia

**TOP BIOTECHNOLOGY CROP PLANTINGS:** United States, Brazil, Argentina

## 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.

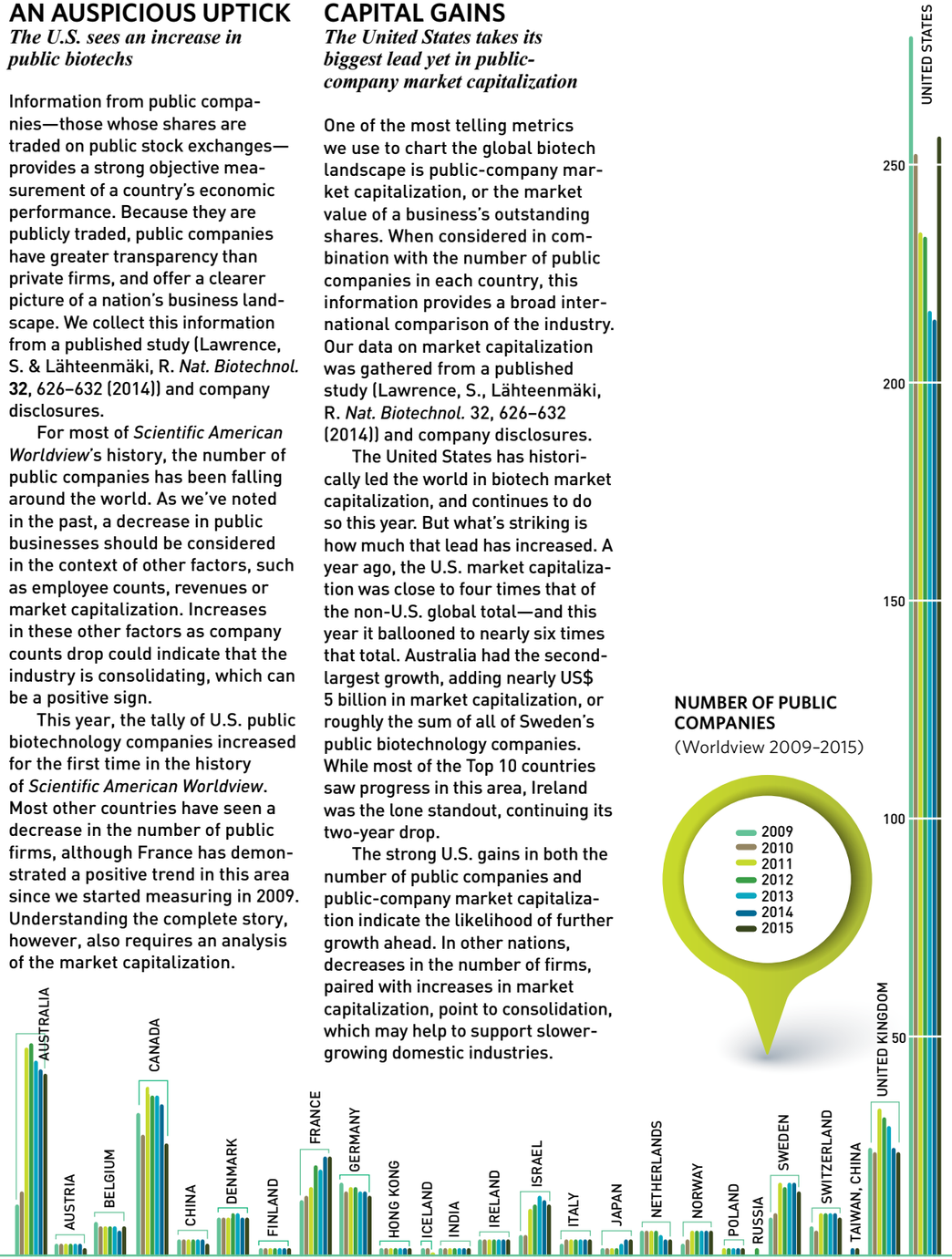
## CAPITAL GAINS

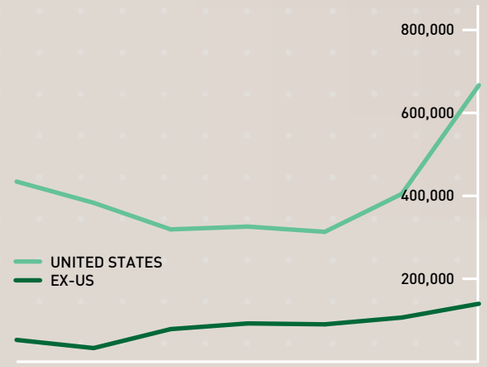
***The United States takes its biggest lead yet in public-company market capitalization***

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.

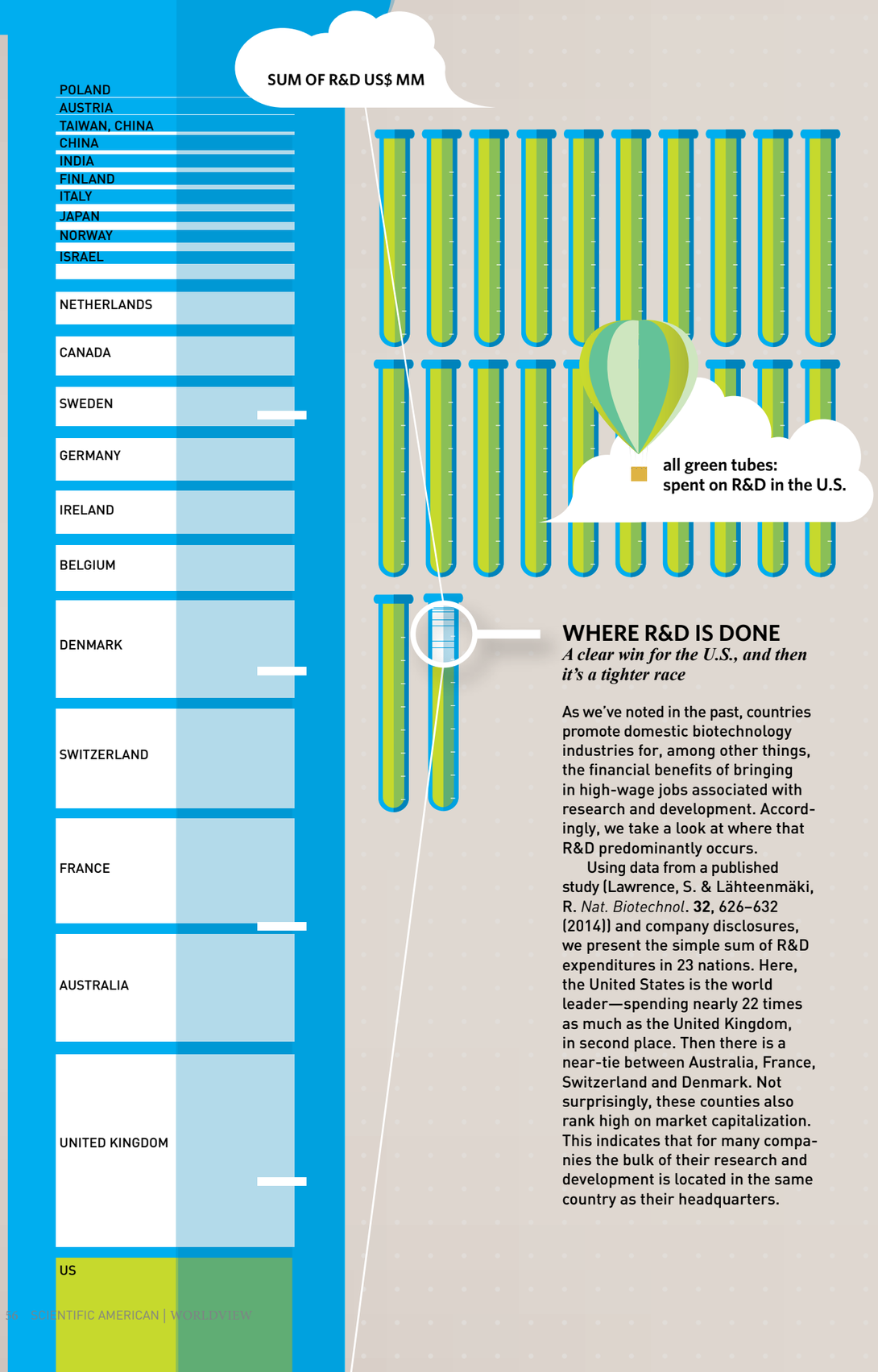
The United States has historically led the world in biotech market capitalization, and continues to do so this year. But what's striking is how much that lead has increased. A year ago, the U.S. market capitalization was close to four times that of the non-U.S. global total—and this year it ballooned 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.




**PUBLIC COMPANY MARKET CAPITALIZATION (US$ MM)**




## 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.

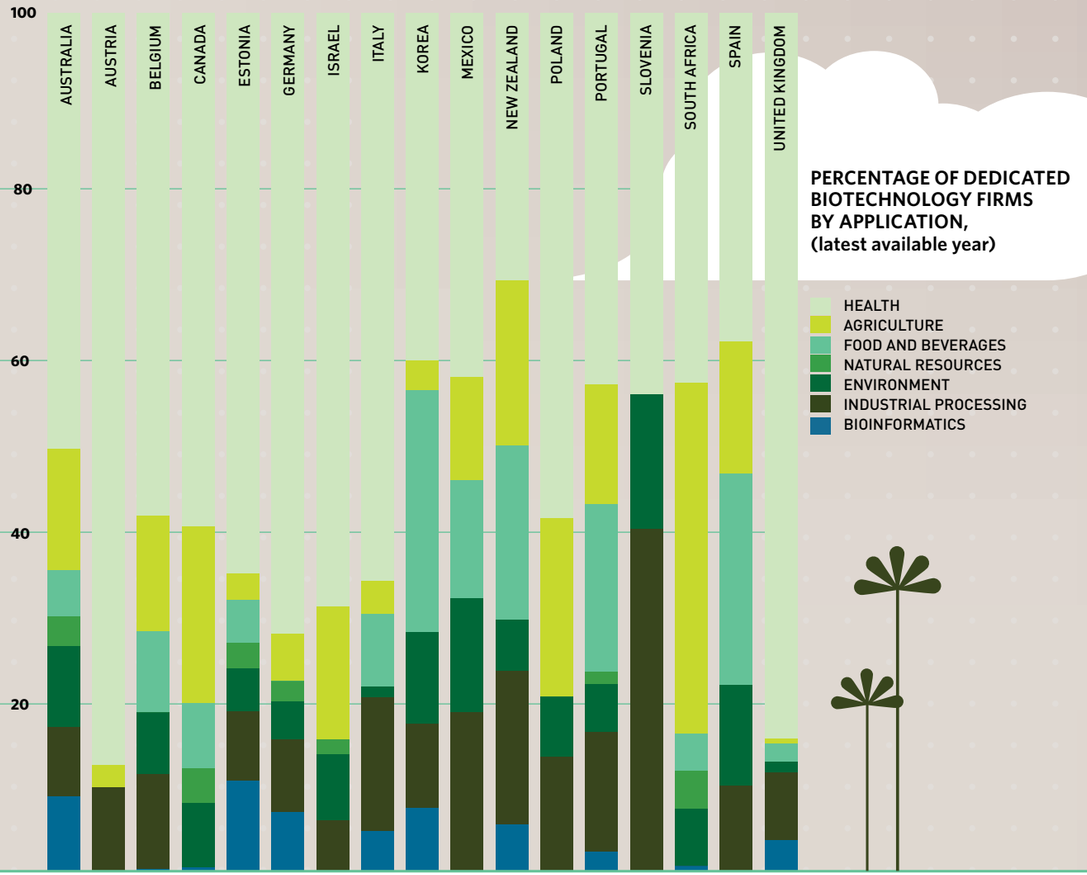
Using data from a published study (Lawrence, S. & Lähteenmäki, R. *Nat. Biotechnol*. **32**, 626–632 (2014)) and company disclosures, we present the simple sum of R&D expenditures in 23 nations. Here, the United States is the world leader—spending nearly 22 times as much as the United Kingdom, in second 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.


## 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 biotech R&D expenditures, respectively. The United States and South Korea were not far behind, with large firms making up 88.4% and 87.7%.

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

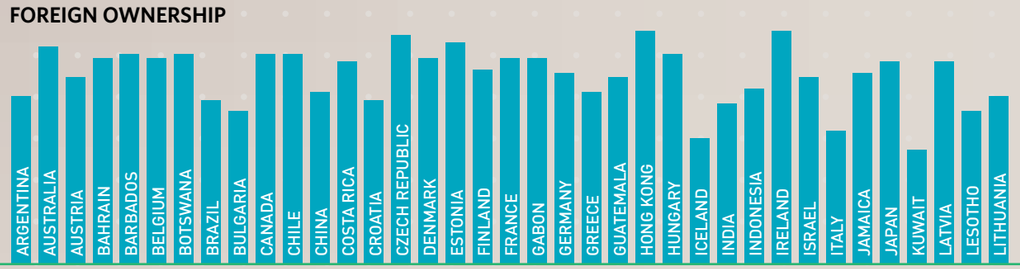
***While biotechnology encompasses many sectors, the most investment is in healthcare***

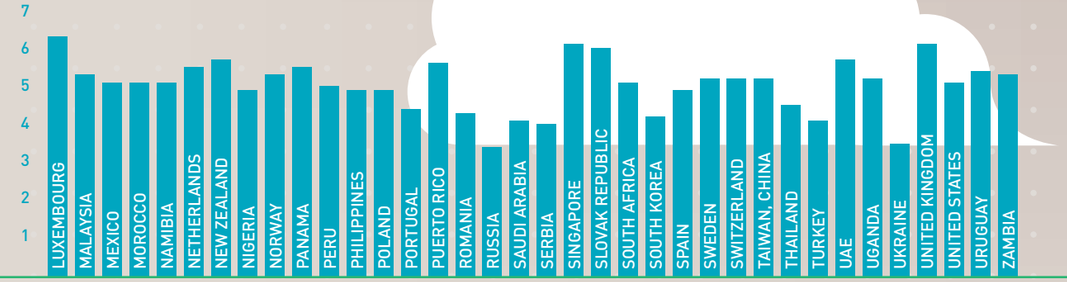
In addition to knowing the size of the companies engaged in biotech R&D spending, understanding the industry also requires an assessment of where the money goes. To find out, we turned once more to the OECD's "Key Biotechnology Indicators" for October 2014, where we gathered data for 18 nations. Spending on biotechnology R&D is divided into seven categories: health, agriculture, food and beverages, natural resources, environment, industrial processing, and bioinformatics.

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 rate—only about 13%—went to industrial processing.

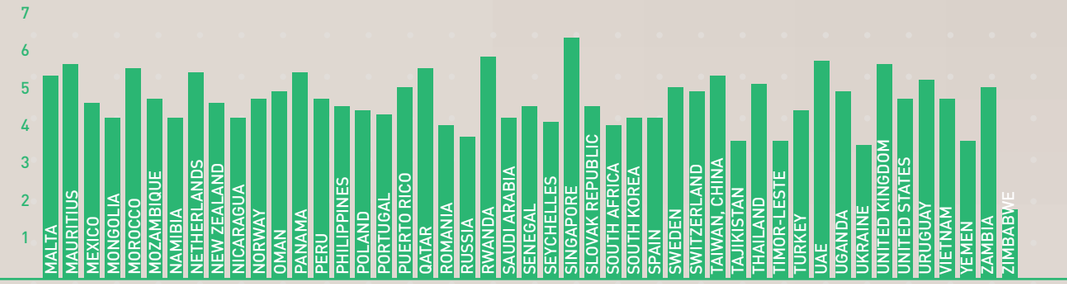
In some nations, biotechnology spending is spread a bit more equally.For instance, New Zealand dedicated about 31% of its R&D expenditures to health applications, and roughly 20% each to food and beverages, agriculture and industrial processing.

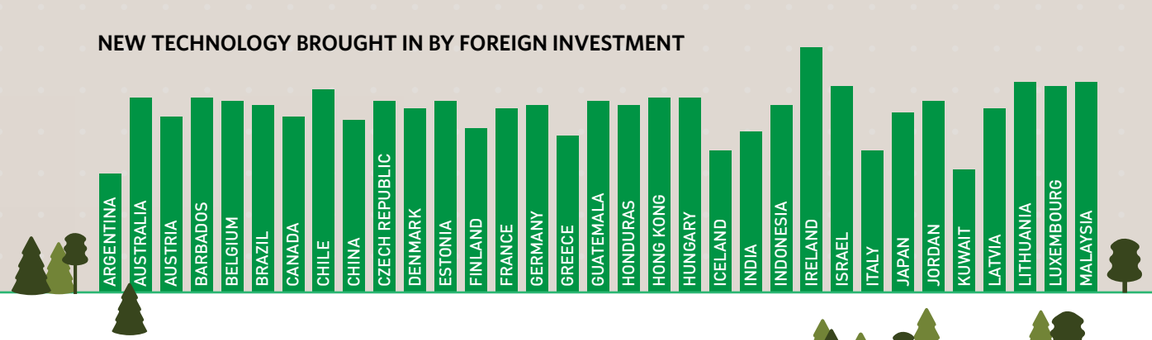
Somewhat surprisingly, bioinformatics receives very little of the funding. In a field that is already very data-focused, one might expect more support of this area. It will be interesting to see if that trend changes over time.

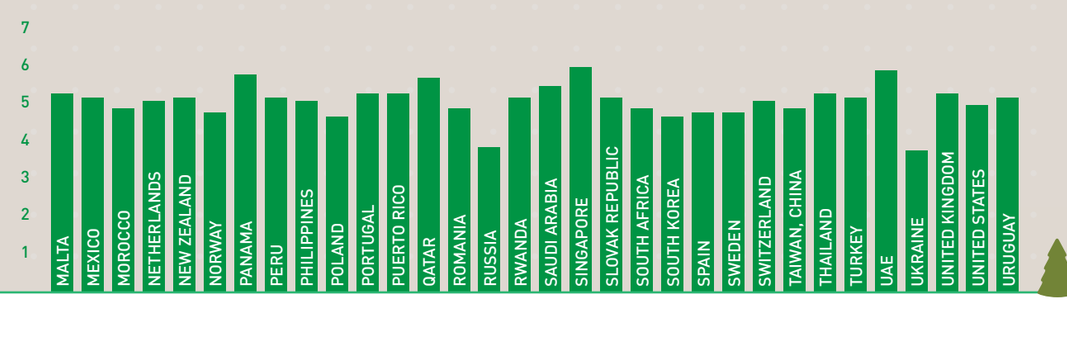







## FOREIGN EXCHANGE

***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.

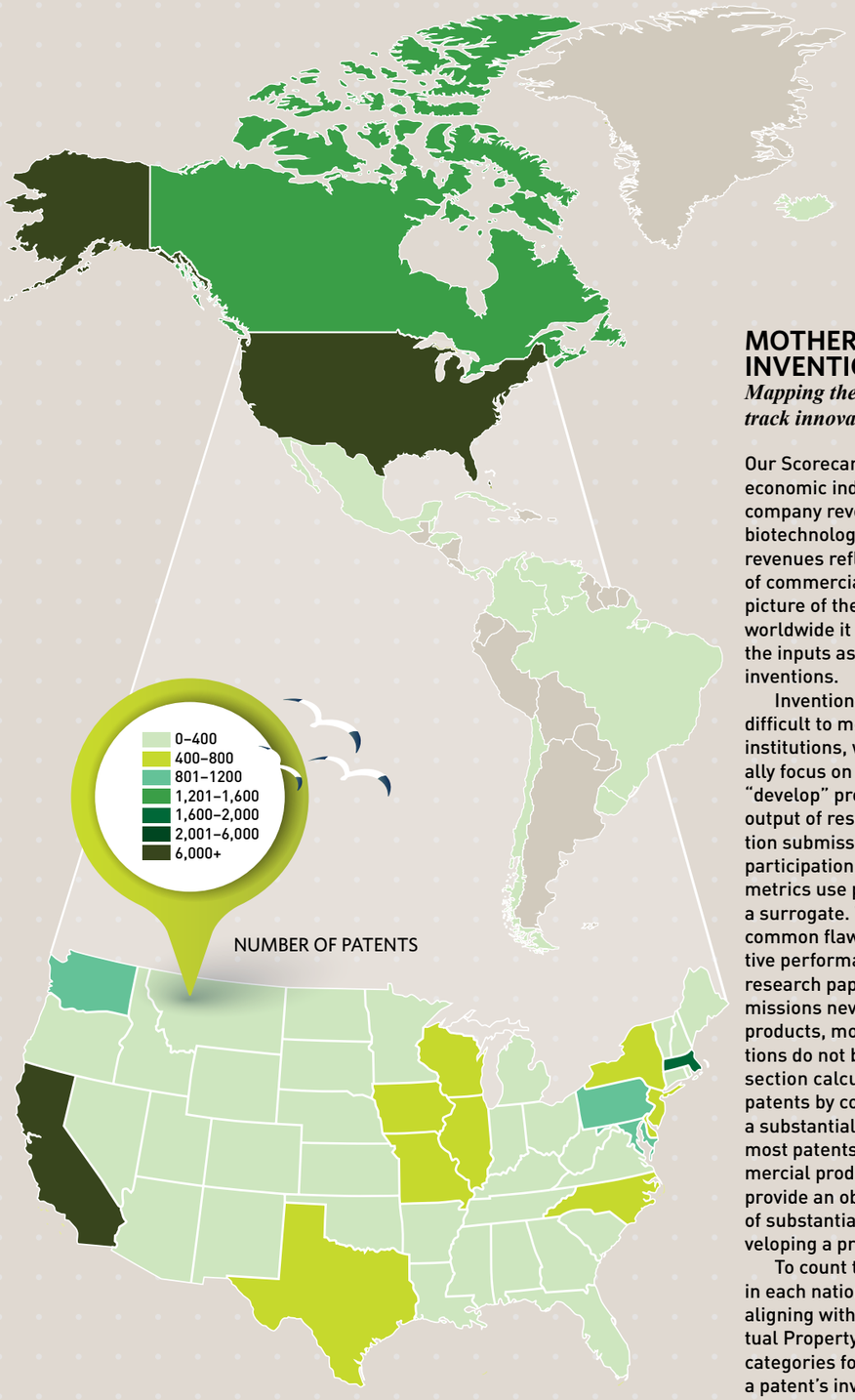
For the prevalence of foreign ownership metric—which is scored from extremely rare (1) to highly prevalent (7)—most of the countries received a 4 or higher. The top score, 6.3, went to Luxembourg, and the lowest, 3.0, to Kuwait.

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.




## MOTHERLAND OF INVENTION

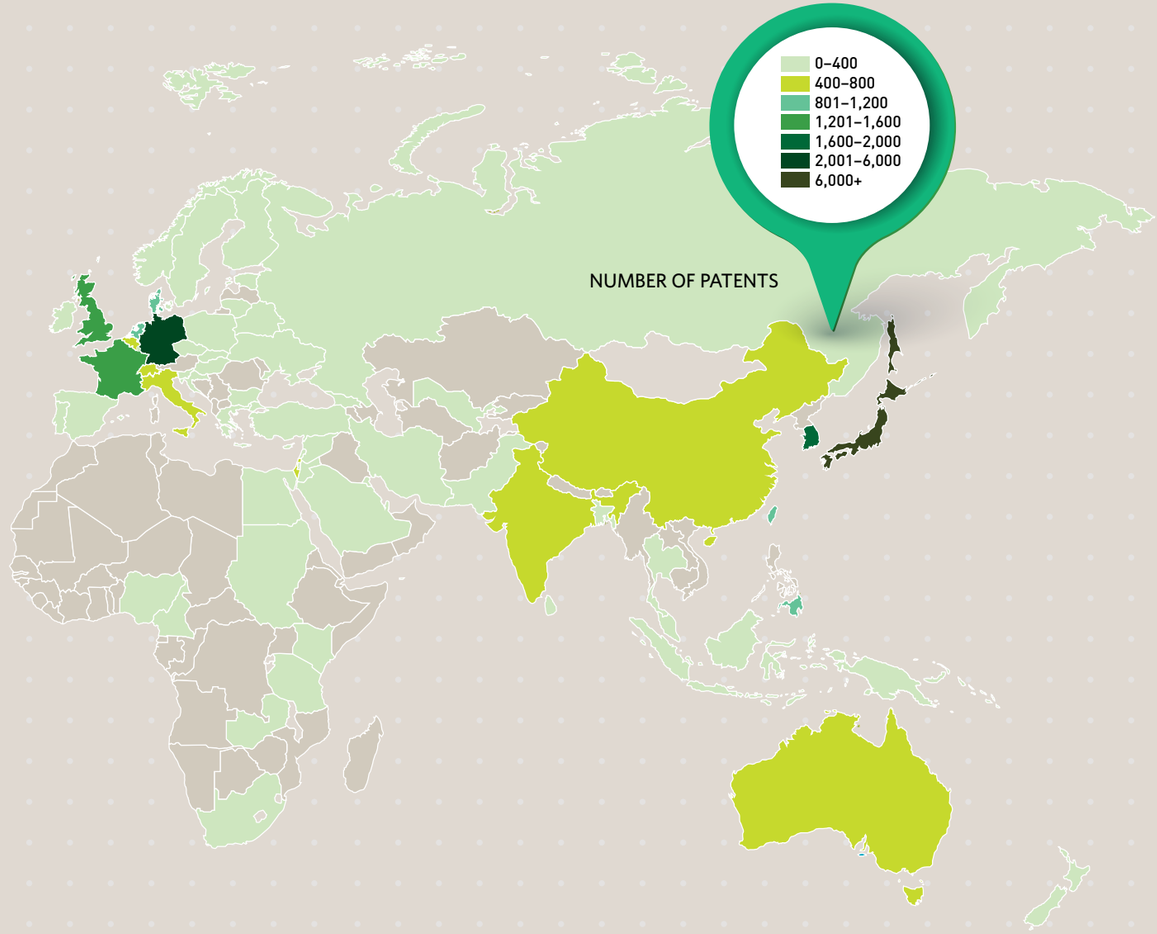
***Mapping the source of patents to track innovation around the world***

Our Scorecard relies heavily on economic indicators, such as public company revenues, to measure biotechnology innovation. But while revenues reflect the final output of commercialization, to get a full picture of the state of the industry worldwide it is critical to consider the inputs as well—especially inventions.

Inventions are notoriously difficult to measure. Academic institutions, which traditionally focus on research and do not "develop" products, might tally the output of research papers or invention submissions to gauge their participation in innovation. Other metrics use patent applications as a surrogate. These methods share a common flaw: they lack an objective performance bar. Just as most research papers or invention submissions never become commercial products, most patent applications do not become patents. This section calculates biotechnology patents by country—which also has a substantial weakness, because most patents never become commercial products—but it does provide an objective measurement of substantial commitment to developing a product.

To count the number of patents in each nation, we identified patents aligning with the World Intellectual Property Organization (WIPO) categories for biotechnology. When a patent's inventors were from the same place, that country received credit for one patent, regardless of the number of inventors. In cases where a patent's inventors came from multiple locations, we assigned inventorship 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 InventorWatch.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.




## BORN IN THE U.S.A.

***Which states generate the most biotech patents?***

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.

## AUTHOR! AUTHOR!

***The highest-ranked nations publish the most***

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 nearly off 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.


## COMPARING COLLABORATIONS

***Leading countries team up the least***

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 directed at locally endemic diseases results in the development of drugs directed at those diseases. Likewise, if tropical countries, for instance, participated more in biopharmaceutical research, then more new drugs directed at tropical diseases would be expected.

While the precise outputs of innovative research projects cannot be predicted (many successful drugs emerge as serendipitous tangents), the location, or context, of the research activities can influence which tangents are pursued. For example, offshoring R&D to emerging economies can lead to knowledge spillovers that seed an innovative industry, and the new enterprises would naturally target domestic needs.

So, simply offshoring research to new locations might produce novel outputs. Accordingly, a shift of R&D away from 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.

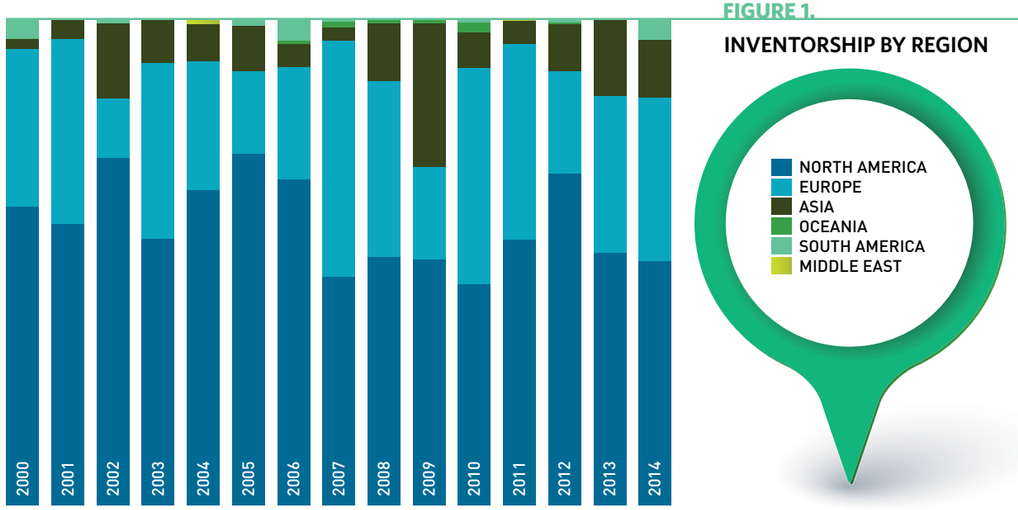



**FIGURE 1.**
**INVENTORSHIP BY REGION**

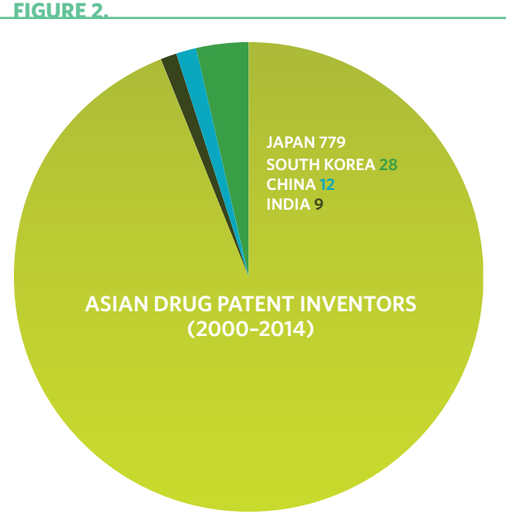



**FIGURE 2.**

## 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."

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

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.***

# 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**

Given the inherent challenges involved in the policymaking 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 biomedical sector? The answer is yes.

A growing body of data shows that there is a positive link between a country's policy inputs—all of 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 for 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 teams often have a candid and 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 Competiveness 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 biopharma?"), 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 coerce localization 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 implemented top-down policies, such as preferential treatment for domestic manufacturers, to meet its Pharma 2020 goals of increasing locally produced medicines and growing export markets. Yet, these policies came prior to adequately addressing areas like quality of manufacturing 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 "struggling 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).

## 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 environment on the number of clinical trials hosted in that country—used as a proxy for biomedical foreign direct investment. We found that nations with weak IP environments, as measured by the U.S. Chamber of Commerce'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 significant 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 example. By some measurements China's IP laws and their enforcement are gradually making strides, 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.

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 investment; rather, the policy environment is an equally, if not more, important determinant. Finally, the outputs themselves, or the lack thereof, actually 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 professor at the University of Maastricht. David Torstensson and Rachel Chu are partners, Amir Dayan is CTO, and Noa Weinstein is a statistician at Pugatch Consilium.***

**BCI OVERALL SCORES & RANKING**

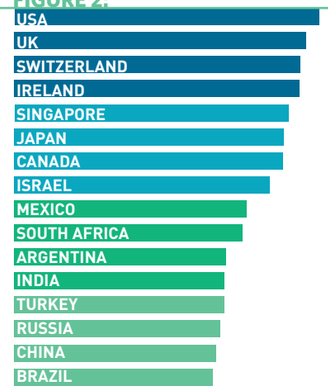
**FIGURE 1:**

| | SCIENTIFIC CAPABILITIES | CLINICAL ENVIRONMENT | MANUFACTURING & LOGISTICS | REGULATORY FRAMEWORK | HEALTHCARE FINANCING | EFFECTIVE IP PROTECTIONS | OVERALL MARKET CONDITIONS | GENERAL CONCLUSIONS | OVERALL SCORE |
|---|---|---|---|---|---|---|---|---|---|
| USA | 13.38 | 11.13 | 12.00 | 11.56 | 10.94 | 13.38 | 12.63 | 1.88 | 86.88 |
| UK | 11.90 | 10.70 | 12.60 | 12.90 | 11.10 | 11.20 | 11.40 | 1.40 | 83.20 |
| SWITZERLAND | 11.06 | 9.89 | 13.00 | 11.83 | 9.78 | 12.22 | 12.06 | 1.72 | 81.56 |
| IRELAND | 10.25 | 9.50 | 13.17 | 12.67 | 10.08 | 11.17 | 12.58 | 1.92 | 81.33 |
| SINGAPORE | 10.71 | 11.21 | 12.29 | 10.43 | 9.07 | 11.43 | 11.71 | 1.29 | 78.14 |
| JAPAN | 9.40 | 10.26 | 11.76 | 11.20 | 8.88 | 12.16 | 11.42 | 1.72 | 76.80 |
| CANADA | 10.32 | 11.07 | 11.54 | 11.21 | 8.86 | 10.74 | 11.18 | 1.64 | 76.56 |
| ISRAEL | 10.21 | 10.64 | 11.29 | 9.39 | 9.39 | 9.79 | 10.50 | 1.64 | 72.86 |
| MEXICO | 7.50 | 10.21 | 9.64 | 8.64 | 8.71 | 10.07 | 9.86 | 1.57 | 66.21 |
| SOUTH AFRICA | 7.21 | 10.00 | 10.50 | 8.86 | 6.64 | 10.71 | 9.57 | 1.50 | 65.00 |
| ARGENTINA | 8.29 | 9.36 | 8.50 | 8.14 | 9.29 | 7.50 | 7.86 | 1.36 | 60.29 |
| INDIA | 6.94 | 9.17 | 10.00 | 8.56 | 6.61 | 8.00 | 9.11 | 1.56 | 59.94 |
| TURKEY | 6.11 | 10.11 | 10.18 | 8.14 | 7.14 | 8.46 | 8.43 | 1.36 | 59.93 |
| RUSSIA | 6.58 | 9.67 | 7.58 | 7.63 | 7.38 | 9.42 | 8.96 | 1.42 | 58.63 |
| CHINA | 7.73 | 7.92 | 8.62 | 6.69 | 7.42 | 8.19 | 9.38 | 1.65 | 57.60 |
| BRAZIL | 4.93 | 7.86 | 8.79 | 7.93 | 7.57 | 9.00 | 9.00 | 1.50 | 56.57 |

**BCI RESULTS BY CATEGORY**

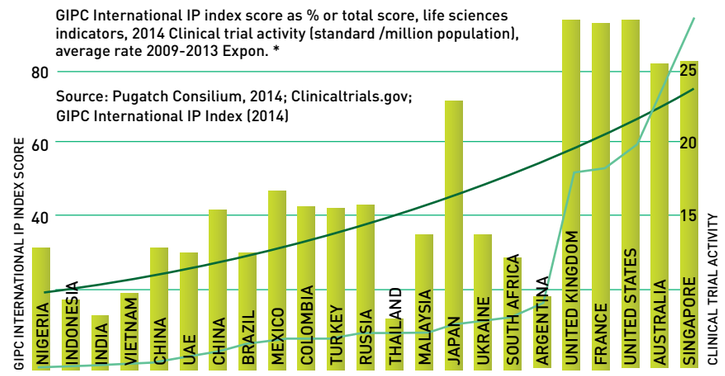
RELATIVE COMPETITIVENESS
STRONGLY COMPETITIVE
REASONABLY COMPETITIVE
LIMITED ABILITY TO COMPETE
STRUGGLING TO COMPETE

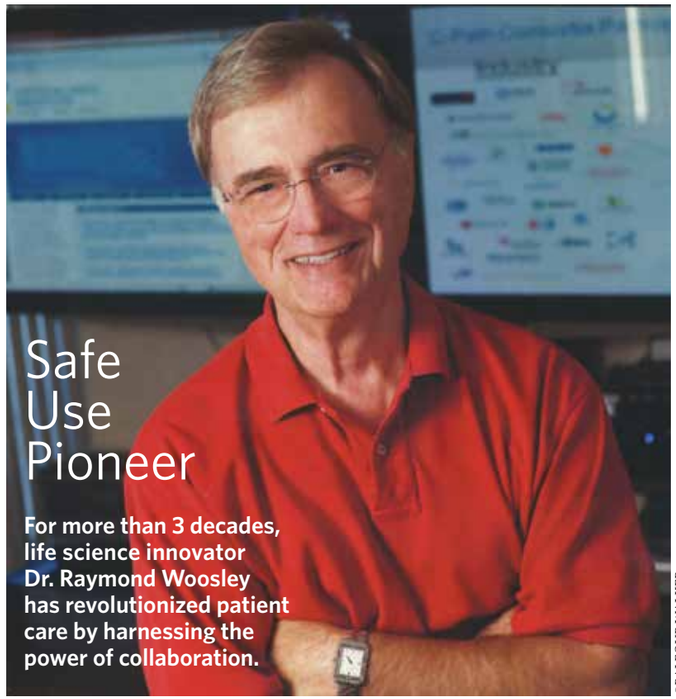
**FIGURE 2:**




**THE IP POLICY ENVIRONMENT IMPACTS INVESTMENT: ASSOCIATION BETWEEN THE LEVEL OF IP PROTECTION & CLINICAL TRIAL ACTIVITY** (as measured by the annual rate of new clinical trials, 2009–2013)

**FIGURE 3:**





# Safe Use Pioneer

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

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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 the Critical Path Institute and CredibleMeds—both of which are guided by the concepts of collaboration and data sharing.

CredibleMeds began as part of 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 with 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.)

***"AZCERT's concept for 'Auto-Pilots' is a novel integration of innovative technologies that furthers the FDA's mission to reduce preventable harm from medicines."***
***—Ali Mohamadi, M.D.***

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 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 concludes from his office in Oro Valley, Arizona, where he works closely with scientists in the local Sanofi and Roche-Ventana facilities. "I feel like 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."

## PRESCRIBING WITH A MEDICATION SAFETY AUTO-PILOT:

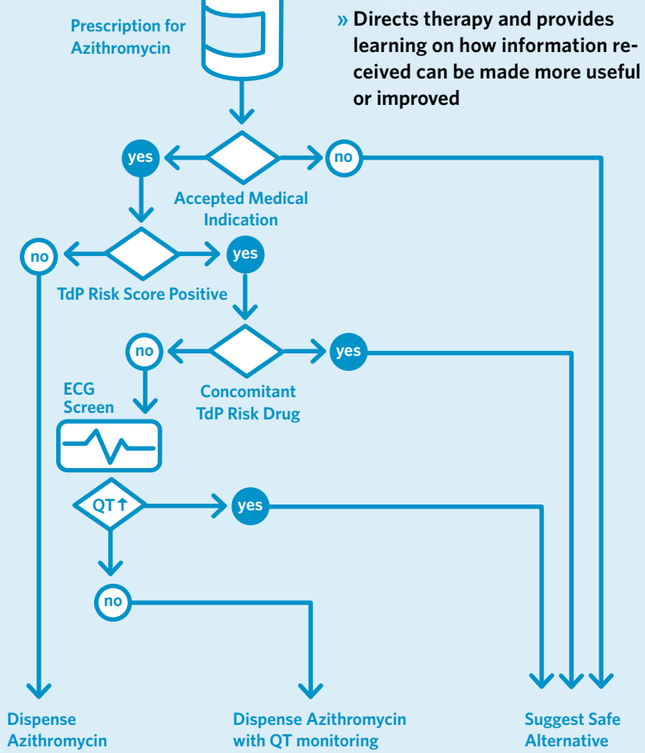
**An actionable, attainable step towards truly personalized medicine is the "Auto-Pilot" system envisioned by Dr. Raymond Woosley and being developed under AZCERT's contract with the FDA's Safe Use Initiative. The Auto-Pilot considers multiple factors in real time and provides the doctor and other healthcare 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)**

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

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



# 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 on an unsuspecting victim. The crowd gathered there that night to learn how sophisticated research from dedicated and driven 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 Colorado 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-engineers 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."

**SUPER SIMULATIONS** For decades healthcare experts predicted that computers would transform the field, but until Colin Hill came along we did not know precisely how. Hill is combining computational physics, systems biology and personalized medicine to completely rewrite the way that clinical trials are done. Instead of running them in people, he plans to simulate them in computers.

That night in California, I asked Wuest: "Why test a drug in a computer?"

"You can gain a lot of insights," she answered, "and there are more opportunities to study disease on a holistic level in ways that are cheaper and in ways that are faster because we can take in data that's already being collected in the healthcare system." That information can then be used to find just the right treatment for each individual patient.

**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 that 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."

**NATURAL HEALING** As Abbate noted earlier, the "tweaking" of natural processes can lead to innovative discoveries, which was the case for Bob Hariri. "We realized probably 20 years ago that for cellular medicine to have a meaningful impact on patients' lives we were going to have to identify a reliable, renewable source that could be turned into a product and put into the hands of physicians—sort of the same way we provide them with pharmaceuticals," he said.

While working as a neurosurgeon, he realized that stem cells would be particularly useful in treating head and spinal cord injuries, but he needed a source of them. So he turned to what he called "the leftovers of full-term healthy pregnancies, namely, the placenta." He added, "This organ is nature's stem-cell factory."

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

**NEVER GIVE UP!** When I asked the panel how we can be sure to keep innovation moving forward, June replied that scientists must be stubborn. "Basically, I tell people when they start in my lab that you have to expect 90% of the time—at least—you are going to fail, so if you're playing baseball, that means you bat 100," he said. "You have to get used to that, but when you do get something that works it's an amazing thing."

The things that work change lives (see "Marathon Man" and "Saving Dolphins Despite Disease"). As Hariri said, "I am moved and compelled by each story where the investment and the time of creating a new drug, a new therapeutic, has transformed those individuals' lives."

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.

## INNOVATOR ALLEY

*Scientific American Worldview* and The Center for Medicine in the Public Interest recognized eight "Top Medical Innovators." Each of them 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**:


### IANNIS AIFANTIS 5

**Professor and Chair**
**Department 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.

### JAMES ALLISON 6

**Professor**
**Department of Immunology**
**Executive Director of the Immunotherapy Platform**
**University of Texas**
**MD Anderson Cancer Center**
**Houston, Texas**

Allison showed that blocking CTLA-4 on T cells can cause them to fight cancer more effectively, and this work led to the drug ipilimumab, which is FDA-approved to treat metastatic melanoma.

### SUSAN DESMOND-HELLMANN 3

**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 7

**Professor**
**University of Colorado**
**Denver–Anschutz 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 4

**Chairman**
**Celgene Cellular Therapeutics**
**Warren, 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 1

**CEO and Cofounder**
**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 8

**Richard W. Vague**
**Professor in Immunotherapy**
**Department of Pathology and Laboratory Medicine**
**Director of the Translational Research Program**
**University of Pennsylvania's Perelman School of Medicine**
**Philadelphia, Pennsylvania**

He 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. Recently, he reported on a study in which this treatment put 35 out of 39 children with leukemia into complete remission.

### CHRISTOF VON KALLE 2

**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.

**PATIENT CASE STUDIES: Innovation In Action**

## MARATHON MAN

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

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 therapy 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."

## SAVING DOLPHINS DESPITE DISEASE

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

In 2000, life couldn't have been better for life-long 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-killing response, 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.

COUNTRY SPOTLIGHTS

ILLUSTRATIONS BY NICOLET SCHENCK

# GREAT STALL OF CHINA

*Regulatory paperwork further slows drug approval*

**BY REBECCA KANTHOR**

Patience is a necessity for pharmaceutical companies seeking to bring drugs to market in China. Last year, the six-to-eight-year drug lag these firms have had to contend with was lengthened another two years. "A lot of products were asked to queue in the line again 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.***

Indeed, the CFDA is playing catch-up with the pharmaceutical R&D industry. Whereas in the past it reviewed mainly generics, since China joined the World Trade Organization in 2001 the agency has seen an enormous increase in the registration of innovative medicines. "Now they have their own R&D pipeline from China and around the world," Cho says. "They need to be able to cope with the advancement of the pharma R&D here. That is a very huge challenge."

Last year, the 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 pharma is 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*

**BY KEREN SOOKNE**

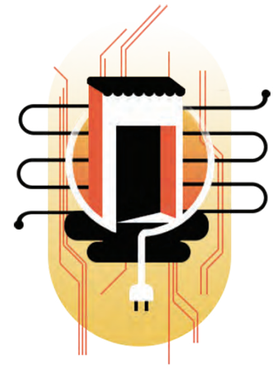
Despite numerous scientific studies demonstrating the benefits and risks of genetically modified (GM) crops, they continue to be the subject of vehement debate. Low levels of public trust regarding GM crop safety present a major problem for experts and governments, as the demand for technological advances focused on food security has never been more pressing. Seeing a need for an objective breakdown of the facts, Matin Qaim, an agricultural economist at the University of Goettingen, Germany, and his colleague Wilhelm Klümper 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 69% 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 agronomy 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**

By 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 frittered 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 to empower individuals. This means linking agro-scientists and technological engineers with local farmers and entrepreneurs, digitally educating the under-educated and creating responsive and transparent civil institutions that can be accessed and monitored 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, overwhelmingly, 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 bullet 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.

***India faces an arduous road ahead, but the significance of Modi's undertaking cannot be overstated.***

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 still doesn't have the right tools. That is where and why we focus our work."

The project was originally conceived by Tachi Yamada, 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 by persuading Japan's foreign and health ministries to finance half of it. The remainder is currently backed by six Japanese pharmas, the Gates Foundation and the United Nations Development Programme.

Although the GHIT doesn't seek financial returns, awarded developers must show that their potential products are innovative, feasible, cost-effective and accessible to the poorest of the poor. The fund's investment covers drug discovery to clinical testing, and it opens the door to access Japan's vast chemical compound libraries, which have not yet been screened for their potential to tackle the diseases that the program addresses.

Slingsby says the fund's model of driving open innovation with good governance is changing the Japanese culture of innovation. To avoid any conflict of interest, for example, representatives of pharmaceutical companies are excluded from GHIT'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, deep-seated in social responsibility and hold a rich chemical library." He adds, "We share the same sense of responsibility and strong willingness to work together."

## GREEN SKIES AHEAD

*Norwegian wood may power tomorrow's air travel*

**BY NANCY BAZILCHUK**

With more than 2,500 kilometers of coastline rumpled by deep fjords and rugged mountains, Norway seems tailor-made for the airline industry. In fact, industry experts are known to joke that "When God created Norway, he was thinking about aviation."

Now, a coalition of forest industry representatives, 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 40% 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.

***"When God created Norway, he was thinking about aviation."***

Norway's first two biofuel flights "were important to show people that this was possible, because there are a lot of myths about biofuels," says Kåre Gunnar Fløystad, an adviser at ZERO, a Norway-based nonprofit that promotes cuts in greenhouse-gas emissions, and which helped organize the flights. Among the passengers traveling from Bergen to Oslo was Tine Sundtoft, Norway's Minister of Climate and Environment. While she was impressed with the flight, she said that the government would be reluctant to unilaterally require Norway's airlines to use a biofuel blend, because it is at least double the price of conventional jet fuel.

In spite of the costs, the Lufthansa Group, SAS and KLM have signed an agreement to purchase biofuel from the Oslo Airport refueling facility. Avinor, the government-owned company that runs 46 of Norway's 52 airports, will subsidize the cost of the biofuel, says Olav Mosvold Larsen, senior executive advisor at Avinor. Biofuel users will also avoid Norway's US$0.13 per liter carbon tax on domestic jet fuels, he says.

One potential source of biofuels is wood, says Erik Lahnstein, executive director of the Norwegian Forest Owners Federation, which represents 36,000 landowners and roughly 70% of the country's forest production. As demand for paper products drops, the industry has closed mills and factories.

Two recent initiatives are intended to pave the way for Norway's domestic production of wood-derived biofuels. The renewable-energy company Statkraft and the Swedish forest company Södra are exploring biofuel production at a former cellulose factory in Hurum, while Avinor has pledged roughly US$12 million over 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 future world," Larsen says. "We just have to make sure it is as sustainable as possible."

## BETTING ON BIOSIMILARS

*A Polish pharmaceutical company scales up to meet the demand in a burgeoning market*

**BY KARYN HEDE**

Just as generic versions of small-molecule drugs have helped to reduce health-care costs, biosimilars offer an alternative to the class of medications known as biologics. Unlike small-molecule drugs, which are derived from chemicals, biologics are produced from living cells. Generic-like versions of biologics are called biosimilars because they work like their patented counterparts, but—unlike generics—can have small structural differences. Over the next decade, biosimilar drugs may well provide substantial price and market competition for biologics, which made up a US$170 billion industry in 2013 and ranked among the world's most profitable drugs.

Many biologic drugs will soon lose patent protection in Europe and the United States, opening the door to manufacturers poised to bring biosimilar versions to market. Europe has been at the forefront of the biosimilar industry, adopting a regulatory framework in 2005. The European Medicines Agency (EMA) has approved 20 biosimilars, and the U.S. Food and Drug Administration approved its first biosimilar product, a version of the white blood cell–boosting filgrastim, in March 2015.

Looking to capture the biosimilars market in Eastern Europe, Polpharma, Poland's largest manufacturer of generic pharmaceuticals, has invested in an R&D laboratory and facility capable of manufacturing clinical-grade biosimilar drugs. Located in the Gdansk Science and Technology Park, Polpharma's biologic unit hopes to register four or five biosimilar drugs with the EMA in the next few years, according to Klaus Martin, the company's head of biologics.

***Over the next decade, biosimilar drugs may well provide substantial price and market competition for biologics.***

"Like generics, biosimilars are very important to rein in health-care spending and allow wider access to drugs," he says. Currently, the firm has a proprietary portfolio, but Martin says at least some are monoclonal antibody drugs that will soon be coming off patent. "I'm quite confident that Polpharma can deliver 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 fermenters and fixed stainless steel pipes that required time-consuming and expensive work stoppages to clean and maintain. In contrast, modern cell-line technology uses smaller-batch, flexible systems with sterile, single-use disposable fermentation 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-engineer their cell lines to achieve higher productivity with existing biologic drugs, because doing so would entail new rounds of expensive clinical trials to show biosimilarity to their earlier production lines.

In addition, lower upfront costs allow Polpharma to produce these medicines at a reduced price, which should offer further financial relief for patients and healthcare providers worldwide.

## REDEFINING ROMANIA

*Generating the infrastructure and financing to establish a vital biotech presence*

**BY BACHIR ABI SALLOUM**

In 1916, Romanian physiologist Nicolae Constantin Paulescu developed a pancreatic extract that was an early version of the life-saving insulin used to treat diabetes. Although he was not among those honored with the 1923 Nobel Prize for the discovery of insulin, experts have since contended that Paulescu was robbed. Some say that his accomplishment stayed hidden while World War I ravaged his country. Whatever the reason, it remains clear that the Romanian scientist was not sufficiently recognized for his contributions to the field. And today, as Romania makes significant strides toward building a dynamic biotech industry in the region, its efforts have gone similarly unnoticed by the rest of the world.

In a concerted effort between government agencies, academia and private companies, Romania has grown its biotechnology sector with research centers in Bucharest, Cluj-Napoca, Brasov and other cities. But the first dedicated biotechnology cluster in Romania—and southeastern Europe for that matter—is bioROne in Iaşi, located in the northeastern part of the country.

Researchers at bioROne focus on biomedicine, including bioinformatics and biopharmaceuticals, genetic testing and gene therapy. In the past five years, scientists there have been granted 100 patents, and the center's cumulative budget during that period was about US$56 million.

Truly a collaborative venture, the cluster was launched by a group representing the country's leading universities, research centers, industry members and other key organizations. Among the 12 founding partners are the Grigore T. Popa University of Medicine and Pharmacy Iaşi, the Institute of Macromolecular Chemistry "Petru Poni" Iaşi, the Institutul Naţional de Cercetare-Dezvoltare pentru Fizică Tehnică Iaşi, the clinical hospitals Spitalul Clinic Judetean de Urgente Sf. Spiridon Iaşi, Spitalul Clinic de Recuperare Iaşi and Institutul Regional de Oncologie Iaşi, SC Antibiotice SA, which is the largest Romanian-owned pharmaceutical company, and the public agencies Institutul de Medicina Legala Iaşi and Directia de Sanatate Publica Neamt Iaşi. In addition, bioROne collaborates with international advisors, including the U.S.-based nonprofit Center for Integration of Medicine and Innovative Technology.

Eventually, scientists at bioROne hope to commercialize their laboratory discoveries. In order to develop its own pharmaceutical products, however, the cluster will need far more funding. As it stands its entire annual budget would barely pay for a small fraction of the cost of developing a single drug. Alternatively, bioROne is looking to attract clinical trials or start-ups to the region. To do this, the Romanian government is taking steps to improve its infrastructure, for example, by joining forces with the European Union and the Grigore T. Popa University of Medicine and Pharmacy Iaşi to raise about US$11 million for a research facility in northeastern Romania to be used for preclinical and clinical studies.

Despite Romania's underappreciated status in the biotech field, some metrics do attest to its impact. For example, a search of PubMed revealed more than 500 scientific publications in 2014 based on work carried out in Iaşi. To move from research to commercial results, however, Romania must ensure that the world sees its discoveries—and continue to build an industry that will generate more of them.

## REVOLUTIONIZING RUSSIA

*To embrace its economic future, Russia must let go of its past*

**BY KARYN HEDE**

Many experts wonder what will emerge from Russia's economic turn away from the West. Is its standing among the so-called BRIC nations—the up-and-coming economic powers of Brazil, Russia, India and China—in jeopardy? In the future, will we be discussing the rise of the BICS nations instead, replacing Russia with South Africa, whose growing momentum can't be ignored? And how will Russia's past, with its complicated attitudes toward business and capitalization, affect the country's present ability to cultivate aspiring entrepreneurs from within?

In *Lonely Ideas: Can Russia Compete?* (The MIT Press, 2013), Loren Graham chronicles the brilliance of Russian inventiveness, as well as the nation's continued failure to sustain and build upon its scientific achievements. A leading U.S. scholar on Russian science and technology and a foreign member of the Russian Academy of Sciences, Graham goes on to question whether Russia can reverse its centuries-old pattern of stifling domestic technological progress.

***And how will Russia's past, with its complicated attitudes toward business and capitalization, affect the country's present ability to cultivate aspiring entrepreneurs from within?***

"[Russians] have made the mistake again and again and again of thinking that modernization is the same thing as obtaining technology," says Graham, who is a research

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 its burgeoning 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 Maxwell 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 Russian science, 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 likely maintain the status quo, or as Graham describes it, its "consistent record, both brilliant and dismal."

## SEA OF GREEN

*Seaweed may be the solution for Scotland's natural-products industry*

**BY BILL CANNON**

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. "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 11 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 gelling 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 alginates in the 1880s.

Fowler and Brown support increasing seaweed harvests through the development of sustainable and "extensive farms for biorefining of alginates 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 US$2 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 going-green philosophy. For example, the Scottish firm CelluComp converts vegetable processing waste from carrots and beetroot and other naturally derived waste products 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's 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 academics. "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 seaweed, its most abundant and undulating of natural resources.

## FROM CRAB TO LAB

*Fighting infections the natural way*

**BY BILL CANNON**

More spider than crustacean, the horseshoe crab resembles a tarantula wearing an old army helmet. It's a living fossil, its basic design unchanged in 440 million years. And the Atlantic horseshoe crab, *Limulus polyphemus*, can survive out of water for weeks, on beaches from Maine to the Yucatan. 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 US$1 billion-plus global contract research organization with headquarters in Wilmington, Massachusetts—is remarkable at detecting harmful impurities in pharmaceuticals and medical devices.

***That blue blood is remarkable at detecting harmful impurities in pharmaceuticals and medical devices.***

Charles River has built its endotoxin and microbial detection business 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 70 parts per billion, "will make a person sick." Limulus blood clots when it encounters 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 renewable 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

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# 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 on genomes 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 treatment 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—looked a lot 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 stem cells that can be turned into treatments.

**Living well into our 90s lies just ahead, if we keep fine-tuning the right tools.**

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 repair and renew itself. What's fueling that ability? Stem cells.

These same cells keep us healthy in our youth. Over the years, though, this regenerative "engine" runs lean on fuel, the stem cells. As that happens, the defects of age start to accumulate. In addition, stem cells orchestrate our response to injury, making them perhaps our best defense against disease. The susceptibility to disease thus increases as we age.

## REPOSITORY OF REPAIR

How can stem cells fix things? It's in their DNA, which forms a repository of synthetic repair. Every stem cell contains information, in its DNA, that codes for the production of molecules that guide the signaling and synthesis behind all of the steps that make tissues and organs. In this process, a primordial stem cell undergoes a series of cellular divisions that make it 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.*

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[1]Lichtenberg FR. NBER Working Paper No. 18235. Pharmaceutical innovation and longevity growth in 30 developing and high-income countries, 2000-2009. Available at http://www.nber.org/papers/w18235. Accessed May 2014.

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