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THE LORE OF RED HERRING

In the 1800s, wily British fugitives discovered that rubbing a herring across their trail would divert the bloodhounds in hot pursuit. Later, in debate and detective mysteries, “red herring” described any clever device used to distract people from the main issue. In the 1920s, American investment bankers began calling preliminary investment prospectuses red herrings as a warning to investors that the documents were not complete or final. The documents were distinguished by covers printed mostly in red. In the spirit of full disclosure, the founders of this publication felt *Red Herring* to be an appropriate name for a magazine dedicated to providing a first look at the companies and trends shaping the business of technology.

A Bio-Revolutionary

Can one person change the world? Historians have debated for centuries about the relationship between individuals and their time. Does a hero emerge at just the right moment to lead a movement or does the individual trigger the revolution?

Our cover story this week, “Open Source Biotech” (p. 30), makes a compelling case for the power of the individual. Molecular biologist Richard Jefferson discovered some of the key technologies that make agricultural biotech possible. Some of his inventions have been licensed by Monsanto and other agro giants. He’s also given his intellectual property away to the less moneyed, once trading a license for enough money to buy a used guitar.

Mr. Jefferson’s radical idea is that too many of the tools used to develop biotech products are proprietary—and often too expensive. Too many patents are issued for products of doubtful originality. That limits who can afford the tools and, therefore, the number of new innovations that emerge.

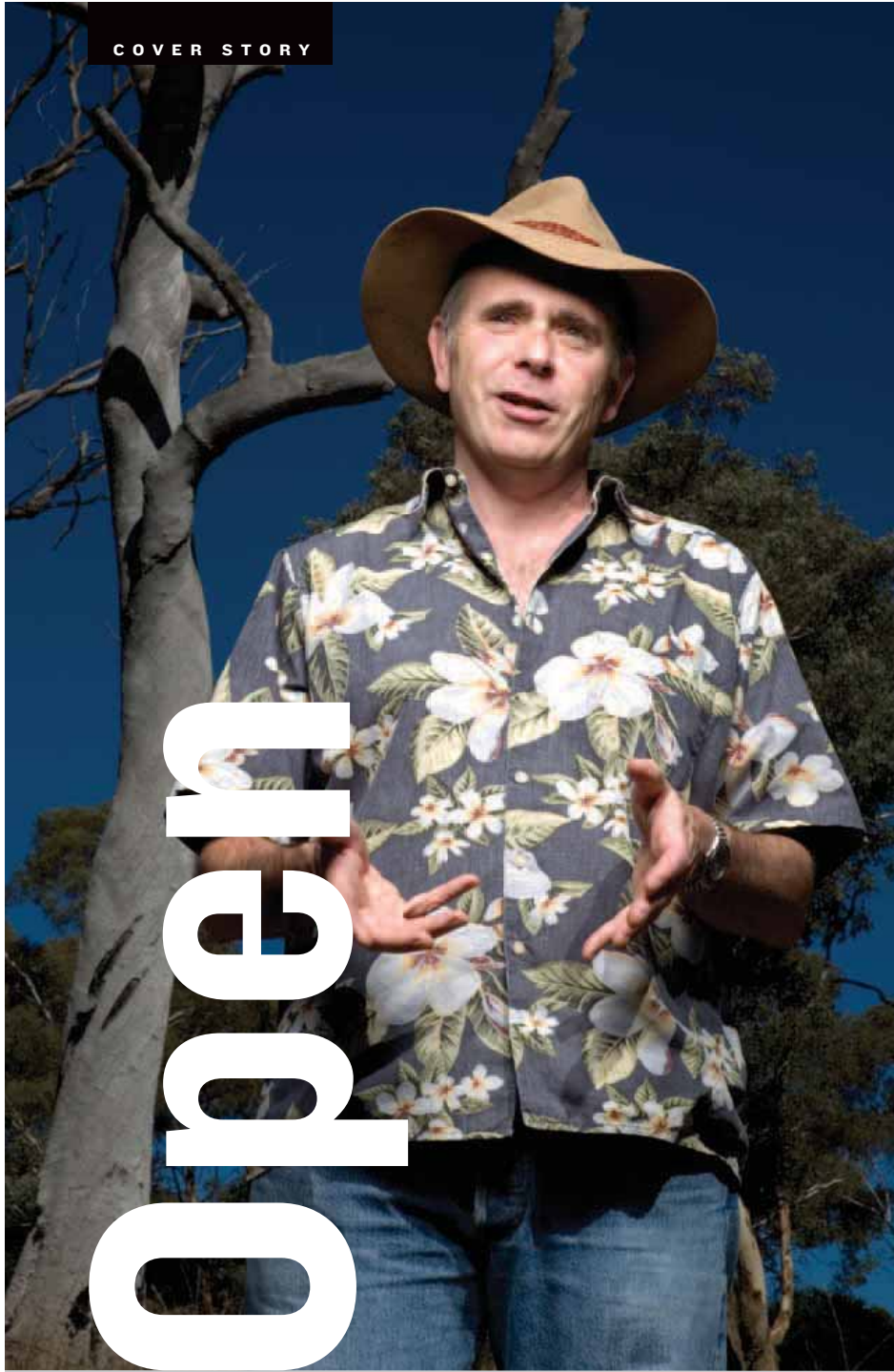
Borrowing from software’s open-source movement, Mr. Jefferson proposed to create a database of patents that are freely available to researchers. He has created a nonprofit organization in Canberra, Australia, to promote his ideas and to marshal his fledgling open-source biotech movement.

Using the language of software, he argues that he wants to share the “operating system” of biotechnology so that real innovation will occur at the “application layer.” Mr. Jefferson is not belittling intellectual property. He just thinks that freeing up the tools that make new discoveries possible will spur a new wave of innovation that has real value.

No need to point out that his argument is not being embraced universally. If there is to be an open-source biotech movement, he will have personally pushed the boulder up the hill. But Mr. Jefferson makes such a compelling case that even those who are not inclined to help him push may find themselves leaning in his direction. **RH**



Joel Dreyfuss, Editor-in-Chief



Borrowing the software model to spur innovation in life sciences finds common ground with IT.

Australian Richard A. Jefferson, an American-born molecular biologist, is out to increase innovation in the life sciences by applying software's open-source model to biotechnology. His goal is to change the global patent system and how people use intellectual property, and break the grip that the big multinationals hold on the tools of innovation.

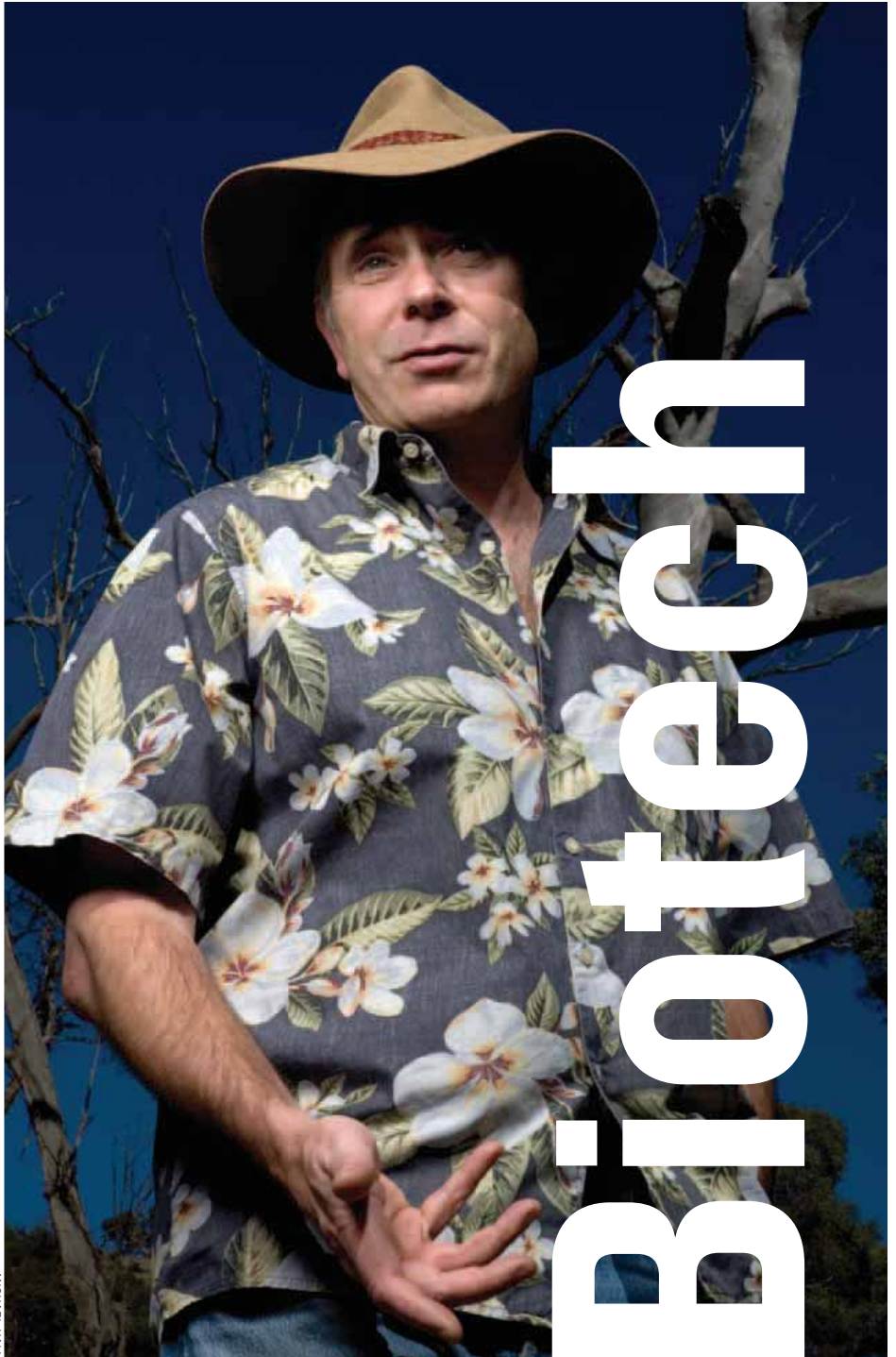
Supporters and critics alike believe he has

a decent shot at succeeding. But just how far and fast he can push the open-source biotech movement is still an open question.

Mr. Jefferson, the man credited with inventing one of the main tools used in plant genetic engineering, started his campaign in 1987 by doing what the big companies that dominate agricultural biotech rarely do: He shared his discovery of beta-glucuronidase gene (GUS), an indicator that tells where a gene is, how much it expresses, and when it acts.



MICHAEL HALL



Biotech

“Patent transparency is the lifeblood of the new open source.”

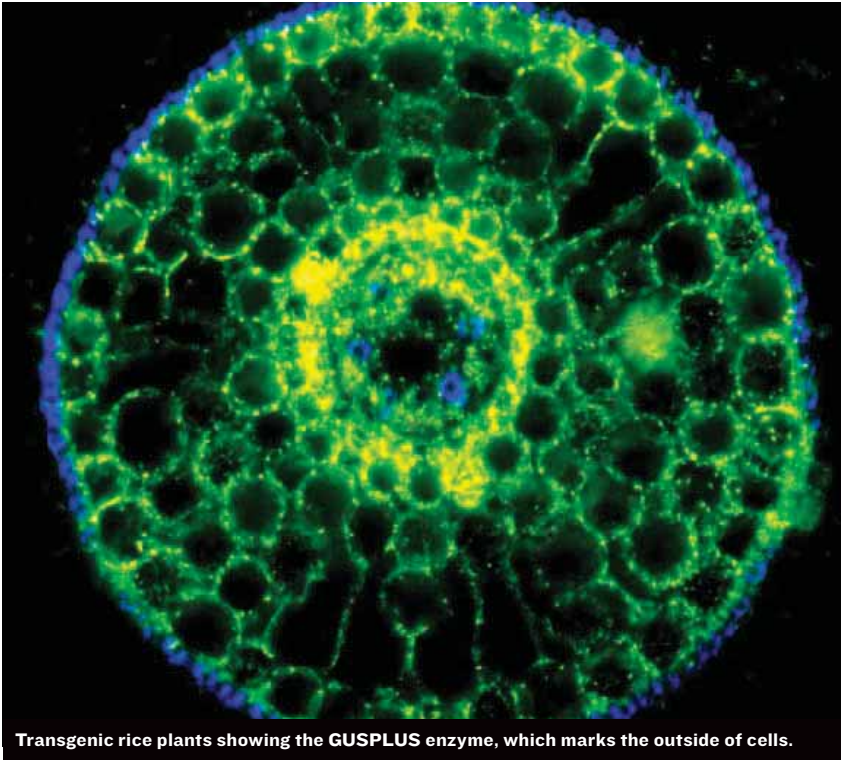
**RICHARD A. JEFFERSON,
FOUNDER, CAMBIA**

GUS is widely credited for enabling many breakthroughs in plant biotech, including the development of one of Monsanto’s first and most profitable agricultural products, Roundup Ready soybeans. Mr. Jefferson first provided GUS and all the know-how to use it for free to hundreds of labs around the world.

When he secured his patents, he charged only what people could afford: Monsanto, he says, paid a substantial amount; academics and companies in the develop-

ing world, including those who wanted to use his work for commercial purposes, received it free of charge. One small company in California got to use his invention in exchange for enough cash for Mr. Jefferson to buy an old Martin guitar.

Mr. Jefferson invested the money earned from GUS in Cambia, a nonprofit institute in Canberra, Australia. The Australian capital became his base for shaking up the biotech sector and making waves in innovation and patent policy. The lesson Mr.



Transgenic rice plants showing the GUSPLUS enzyme, which marks the outside of cells.

Jefferson learned from GUS is that freeing the basic tools of biotech—the keys to inventions affecting human and plant—is crucial to spurring innovation.

Had Monsanto or DuPont invented GUS, Mr. Jefferson reckons it would have been a different story. “When big companies invent, discover, or acquire these technologies they rarely use patents to generate and share the next generation of technology.”

If multinationals are allowed to hold patents on basic tools and gene sequences that are the very operating systems of life, promising new sectors will be left undeveloped and society will lose out, says Mr. Jefferson. He is convinced that the open-source movement in software should be applied to agriculture and to drug discovery.

In agricultural biotech, for example, fewer than a half dozen big companies in the United States and Europe own more than 70 percent of the patent rights, including basic tools. “The fragmentation of the remaining patent rights then invites patent trolls and over-valuing, further stalling an already moribund industry,” says Mr. Jefferson.

As much as 20 percent of the human genome is controlled by patents, of which about two-thirds are owned by private firms.

Taking a collaborative open-source approach could speed efforts to reduce

hunger and disease. “It is not about paternalistically saving the third world, it is about changing the practical and normative realities of how innovation is done, is coalesced, and is shared,” says Mr. Jefferson. “That is what will make the difference.”

Sir John Sulston, who won the Nobel Prize in Physiology or Medicine in 2002 for his work on human genome sequencing, says he supports Cambia’s approach to a science commons because he shares Mr. Jefferson’s views that advances are being stunted by the current patent system. Universities, for example, are increasingly looking to make money by patenting technologies that might otherwise have been placed in the public domain for society’s free use, says Sir John. That skews their own research and prevents others from building on their work.

Many scientists see the need for open-source biotech, “so hopefully the idea will catch on,” says long-time Cambia supporter Richard Jorgensen, editor-in-chief of scientific journal *The Plant Cell*, and the discoverer of a breakthrough technology now known as RNAi.

However, some believe that if the open-source biotech movement is to gain credibility and mass appeal, a Monsanto or a pharma company like Merck will have to

take a giant leap, as IBM did when it embraced open-source software, deciding to make money on higher-level applications rather than from basic tools. But it is not clear that drug companies and agriculture product makers are ready to play.

“The problem is dislodging the incumbents who are rich and powerful,” says Columbia University Law School Professor Eben Moglen, general counsel of the Free Software Foundation and director of a nonprofit group called the Public Patent Foundation, which mounts court challenges against questionable patents in pharmaceuticals and other sectors.

Hugh Grant, the CEO of agricultural biotech giant Monsanto, declined to be interviewed. In an emailed statement to *Red Herring*, Monsanto spokeswoman Lori Fisher says, “We think the concept [of open-source biotech] is interesting from an intellectual point of view and reflects the growing consensus that biotechnology has much to offer developing country agriculture.” But, she adds, “Our experience is that intellectual property issues are not the major obstacles to transferring technology, but rather... things like lack of science-based regulatory policy and practices, lack of capacity, infrastructure, and funding to convert good ideas into finished products farmers can plant.”

Treading Lightly

DuPont is taking a wait and see approach, says Ganesh Kishore, DuPont’s vice president of science and technology and chief biotechnology officer.

“I think this kind of open-source approach could well transform the land-

“Discoveries yet to come will be extraordinary but they won’t happen if people lock up intellectual property.”

CAROL KOVAC, GENERAL MANAGER, IBM

scape and advance the rate of progress of innovation, but due to understandable reluctance from established players, I don't know if it will be in as explosive and transforming of a manner as I think Richard would hope," says L. Val Giddings, until recently vice president for food and agriculture of the Washington D.C.-based Biotechnology Industry Organization (BIO), which represents agricultural biotech giants Dow, Bayer, DuPont, Monsanto, and Syngenta, as well as the major pharma companies.

Cambia has already launched a technology development and sharing initiative called Biological Innovation for Open Society (BIOS). The program is a protected commons in which scientists can collaborate and contribute via the Internet. Mr. Jefferson says BIOS is not trying to do away with intellectual property, just proposing a way to share the tools and "operating systems" of innovation. This will allow innovation at the application layer, he argues, but with fair and open competition.

Mr. Jefferson and his staff of 35 at Cambia kick-started BIOS by making all of their technologies freely available under the terms of the group's Biological Open Source license. These include a version of GUS called GUSPLUS and Transbacter, which bypasses the established and heavily patented transformation process for transferring genes into plants.

As it grows, the online BIOS tool kit should allow ag-bio startups to make genetic improvements to neglected crops or solve low-margin problems without signing early-stage licensing or partnering agreements with multinationals currently controlling the genes and the means to transfer plants.

That is important because, for example, a number of patent constraints are preventing the results of research that the Rockefeller Foundation is funding from being developed and disseminated to small-scale farmers, says Gary Toennissen, director of food security at the New York City-based nonprofit. The Rockefeller Foundation is the largest financial supporter of Mr. Jefferson's Cambia initiative.

In many cases big companies, through patents, gain control of the basic tools of doing plant biotech, says Mr. Toennissen, although the tools were developed at universities or public-sector institutions.

While scientists are still allowed to use those tools for research to, say, make

an improved strain of rice, they cannot transfer their invention to public-sector institutions in countries like Vietnam or Bangladesh without first obtaining a license from the patent holder. Often the multinationals have no interest in granting the license because liabilities are high in small-margin innovations, and profits are small or non-existent.

One of the more prominent examples is golden rice, a variety of rice that was engineered to provide dietary Vitamin A to populations in need. Lack of Vitamin A causes roughly 500,000 cases of blindness and contributes to more than 2 million deaths annually. But in translating the research into deliverable plants, the developers encountered more than 70 patents in several countries and six material transfer agreements that delayed the work substantially, Yale professor Yochai Benkler, a proponent of "open innovation," explains in his latest book, *The Wealth of Networks: How Social Production Transforms Markets and Freedom*, due out this month.

While this problem was solved by licensing and concessions from the private-sector players because of golden rice's prominence as a public relations poster child, it did not provide solutions to the industry-wide problem, says Mr. Jefferson.

Cambia is tackling the issue by giving free access to its discoveries, but there's a catch: anyone using the technology has to contribute the improvements to the core toolkit—a model similar to the general public license (GPL) used in open-source software. Mr. Jefferson, in fact, thinks the better analogy is licensing for open-source

As much as 20 percent of the human genome is controlled by patents, of which about two-thirds are owned by private firms, potentially preventing scientists from innovating.

Apache servers, which accommodate downstream private use, a necessary step for securing investment for the lengthy and expensive development process.

Software vs. Biotech

Brian Behlendorf, founder and chief technology officer of Collabnet, a for-profit open-source company in Brisbane, California, and the driving force behind the Apache web server and the foundation that guides it, says that despite important differences he is convinced that the open-source model can work in life sciences. "It just might be harder and take a bit longer," he says. Collabnet, Mr. Behlendorf's company, hosted one of Cambia's services for six months as part of an experiment exploring parallels between the open-source approaches to life sciences and software.

Life sciences are different because patents are more of an obstacle, innovation cycles take longer (a new plant variety or new drug will often not be ready until 10 years after its inception), and the costs of innovations are higher.

And critics say the approach won't work in life sciences because of the expense and specialized equipment needed. Mr. Jefferson argues that there is excessive capacity in the public sector that, when aggregated and focused, can be mobilized for collaborative delivery of outcomes that will help combat malnutrition and major diseases.

Mr. Jefferson, Cambia deputy director Marie Connett, and scientists at major cancer research centers are now discussing collaboration on an open-source approach to cancer diagnosis and therapeutics. Cambia will start things off with its patents on telomerase, an enzyme that restores DNA at the ends of chromosomes called telomeres. Without telomeres, cells cannot divide, and they die. Unlike regular cells, cancer cells keep making telomerase so that they are kept intact. The hypothesis is that blocking telomeres with drugs should destroy cancer cells.

It's a good example of marshaling efforts to solve a problem. More people die from cancer than infectious disease in both the developing and developed world than from infectious disease, yet 4 million die every year because they can't afford medications offered by big pharma, according to Mr. Jefferson. "Imagine it is your mother with advanced breast cancer and she's too poor to pay the \$50,000 for a course of Avastin or Herceptin that

Genentech says it deserves, so you watch her die painfully,” he says. “Now tell me it is not time for some new approaches.”

Opening Up the Data

Creative Commons, which, with the help of Stanford University law professor Lawrence Lessig, has developed an alternative copyright system to make literature, music, film, and scholarship freely available online, supports the idea of applying new approaches to scientific processes. Last year saw the creation of Science Commons, which is trying to expand Creative Commons’ work in the sciences by developing alternative mechanisms to allow universities and industry to share data and intellectual property in a more open manner. Its first adherent, Uniprot.org, which claims to have the world’s most comprehensive catalog of information on proteins, is now using Creative Commons’ licensing.

And, not surprisingly, IBM, which has embraced open-source software and incorporated it into its business model, is supporting the idea of porting the model to basic tools in life sciences. “Discoveries yet to come will be extraordinary but they won’t happen if people lock up intellectual property,” says Carol Kovac, IBM’s general manager for health care and life sciences.

Just as Richard Stallman, founder of the free software movement, campaigns against software patents and extensions of copyright law, Mr. Jefferson is making it his life’s mission to break the grip that big companies have on advances in agricultural biotech and biomedicine.

Besides opening access to diagnostic tools, Mr. Jefferson is out to reform the global patent system so that innovation can flourish and myriad small and medium-sized companies can also make money from their inventions. Mr. Jefferson claims to be a descendent of Thomas Jefferson, who reluctantly created the U.S. patent system as a means of ensuring advances for the public good.

Cambia has created Patent Lens, the world’s largest free full-text database of patents. It will soon allow third-party observations when patents are filed anywhere in the world, giving industry and citizens alike the opportunity to alert patent offices to prior art and warn them when patents are too broad or just absurd. The database, originally limited to life sciences, has just been extended to patents in

Too Good to Pass Up

Universities bring in piles of cash from intellectual property licensing and royalties.

	Total Revenue (millions)	Millions	Percent of Total
Columbia University	\$2,074	\$178.4*	8.6
University of California	\$14,166	\$81.3**	0.57
Stanford University	\$3,475	\$43.3***	1.25
Florida State University	\$2,646	\$35.60	1.35
University of Wisconsin-Madison	\$1,696	\$32	1.89
University of Minnesota	\$1,237	\$38.70	3.12
Harvard University	\$2,473	\$47.90	1.94
Cal Tech	\$531	\$26.7	5.02
All Universities	\$227,000	\$1,270	0.56

Source: *The Wealth of Networks: How Social Production Transforms Markets and Freedom*, by Yochai Benkler

*Estimated because of ambiguity in the technology transfer office’s annual report. **Does not include expenses.

***Almost half of this amount is income resulting from the IPO of LiquidMetal Technologies and does not represent a recurring source of licensing revenue.

all sectors. In time, its reach will include Asia as well as the U.S. and Europe.

Mr. Jefferson says Cambia is in discussions with U.S. and European Union patent offices and the World Intellectual Property Organization on ways to work together. He is also talking with the Open Source Development Lab about improving his organization’s database by leveraging that group’s expertise in software with Cambia’s expertise in patents.

All open-source initiatives—in any sector—depend on total transparency and understanding of patents, he argues. “We can wish they’d just go away as some in the Free and Open Source Software community do, but one patent right withheld can destroy an entire initiative and the confidence of innovators and investors,” Mr. Jefferson says. “Patent transparency is the lifeblood of the new open source and patent reform is a logical consequence of total public transparency and engagement.”


Cambia’s moves come at a time when pressure is growing to change the patent system. Research in Motion’s recent court

battle over its popular BlackBerry wireless email service is just one example. A case argued before the U.S. Supreme Court last month questioned whether the patent for a blood test for a vitamin deficiency was so broadly construed that it included a natural process of the human body, possibly preventing other inventors from developing new and better tests. Another U.S. Supreme court case argued in March involved claims that eBay’s “Buy It Now” features infringe on two patents held by a company called MercExchange.

While IT companies complain that they can be held ransom by owners of questionable patents, Mr. Jefferson and others argue that many lines of research and development are blocked by misuse of intellectual property before work even begins.

Some, like Mr. Moglen, general counsel of the Free Software Foundation, are less optimistic than Mr. Jefferson about the odds that the U.S. Patent offices or others will formally incorporate third-party observations.

It doesn’t matter, says Mr. Jefferson. Cambia’s Patent Lens doesn’t need the immediate buy-in of the world’s patent offices. The datasets are in hand or can be bought. Once patents are harmonized, annotated, properly commented, and linked to prior art, pressure will be brought to bear from the public to only grant valid ones, helping all patent offices to make better and more transparent decisions, he says.

His distant uncle, Thomas Jefferson, would approve, says Mr. Jefferson. The historical Mr. Jefferson established patents solely to further the public good. For the modern-day Mr. Jefferson, ensuring that principle is kept is a matter of unfinished family business. 

“The problem is dislodging the incumbents who are rich and powerful.”

EBEN MOGLEN, PROFESSOR,
COLUMBIA UNIVERSITY LAW
SCHOOL