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Open sesame

At the end of this month, Celera Discovery Systems, the genomic information service of Celera Genomics, is to close its doors. In doing so, the company will release all of its human genome data, as well as some mouse and rat sequences, into the public domain. Although barely registering on news wires or in the press, the announcement has been welcomed by the open-source movement as a triumph of public science over proprietary interests. What's more, calls are growing for the open-source model to be applied to other areas of biotechnology, enabling scientists to innovate, unimpeded by patents, licenses and lawyers—all for the greater public good.

Open source is a style of intellectual property (IP) management that seeks to combine freedom of access and freedom to cooperate for users, with the ability to generate revenue for owners. Proponents of open source say it is needed in biotechnology because certain IP developments, such as the overpricing of stacked license fees and royalties or the concentration of key IP rights into the hands of a small number of powerful corporations, are compromising researcher access to technology.

The model for open-source licensing comes from the free software movement, in which the underlying programming instructions, or source code, for a given piece of software are made freely available. Anybody can look at the code, alter it or improve on it. The twist is that they must also agree to share their modifications with others under the same terms. The best known example of the success of open source is the Linux operating system, which was developed over the Internet by a Helsinki University student, Linus Torvalds, with the help of huge numbers of volunteers.

Richard Jefferson (see p. 643), a biologist who pioneered the development of the β-glucuronidase plant marker system, has been likened to Torvalds as the guru of open-source biology. Jefferson, his startup CAMBIA and an initiative termed BIOS (Biological Innovation for Open Society) are all part of a virtual project development group that shares data and collaborates as if they were all on the same team. Innovators still retain ownership of their own patents, but they can't hinder anybody from creating something from the same core information to develop similar products.

Jefferson rightly points out that the patent landscape in agbiotech has created "real and perceived" obstacles to innovation. Specifically, he has identified as a particular hindrance the raft of patents surrounding the standard industry gene transfer vector, *Agrobacterium tumefaciens*. Last February, Jefferson published in *Nature* (**433**, 629–633, 2005) several alternative systems to *A. tumefaciens,* in what he termed a "shot across the bow of companies that use the patent system to dominate and then destroy an industry."

All of this is good as far as it goes, but there are two central flaws in Jefferson's approach, which seem likely to compromise its success as a model for biotech innovation.

Part of the problem is that there are too many other obstacles to clear in the patent thicket covering the creation of a transgenic plant. For example, to develop Golden Rice (provitamin A transgenic rice), researchers had to navigate more than 40 patents and contractual obligations held by industry and academia. *A. tumefaciens* is just one piece of the puzzle. There are many other aspects key to plant science innovation that are as important, or more so, like selective markers, promoters and gene silencing technologies. Because it's unlikely that open-source approaches can circumvent all of these patents, let alone the gather the manpower to do so, a completely patent-free way of creating a transgenic plant product seems a remote prospect (*Nat. Biotechnol.* **23**, 309–310, 2005).

Perhaps the key difficulty facing Jefferson's open-source model, though, is the lack of a mechanism to drive the initiative forward so that it can compete with commercial biotech patenting. CAMBIA is, for all practical purposes, a virtual organization, formed with a token amount of startup money from the Rockefeller Foundation and IBM. It is not the sum of its parts—it is but one part, and the sum of it doesn't add up to much more than good intentions. Many researchers, CEOs and investors in biotech don't even know that Jefferson, or for that matter open-source biology, exists. With so few resources and such low visibility, and competition from biotech corporations that have established not only funding mechanisms but also a 20-year market monopoly from their patents to bring home the bacon, it is difficult to see how the CAMBIA approach is ever going to get open source off the ground.

What open-source biology really needs is another Human Genome Project. An Apollo project, with some well-defined goal that the government, the public or a large industrial partner can back with sufficient resources to carve out the enabling territory for new medicines that would benefit large, underserved populations in developing countries—the kind that traditional biotech and pharma ignore. In this respect, the commitment last December of a $43 million grant from the Bill & Melinda Gates Foundation to the Institute for OneWorld Health, the University of California, Berkeley, and Amyris Biotechnologies to create a more affordable, accessible cure for malaria shows the way forward. It simply makes no sense for open source to compete head to head in areas of biotech where companies using the patent model already operate.

Open source needs to be recast as a novel alternative that might work in certain, well-defined arenas that lend themselves to the approach. It might well be that only a handful of biotech avenues exist where open source has a shot of reaching its goal of putting enabling science and research tools into the public domain where they will benefit humankind and spur invention.

The Human Genome Project was perhaps the most ambitious open-source effort ever attempted. Yet the only reason it moved forward was because it was bankrolled with tens of billions of dollars from the US government and the Wellcome Trust. Without that gargantuan investment, there would likely be no open, publicly accessible human genome sequence unencumbered by patents. And Celera Discovery Systems might still be in business, selling hapless researchers subscriptions to its proprietary genome database.