

## Tools and Technology | Open-Source Initiative Circumvents Biotech Patents

Researchers develop workaround for *Agrobacterium*-mediated gene transfer | By Aileen Constans

Though agricultural biotechnology has the potential to transform small-scale farming in developing countries, such transformation faces a major bottleneck: the intellectual property landscape.

Courtesy of Brian Weir, CAMBIA



**OPEN SOURCE GOES BIO:** This tobacco seedling, transformed with *Sinorhizobium meliloti*, an alternative to *Agrobacterium*, is stained for  $\beta$ -glucuronidase (GUS) expression.

Though agricultural biotechnology has the potential to transform small-scale farming in developing countries, such transformation faces a major bottleneck: the intellectual property landscape. Case in point: Golden Rice, engineered to produce beta-carotene (a source of vitamin A), is subject to approximately 40 patents that initially hampered its dissemination to developing countries.

Further, if a scientist in the public sector, small biotech company, or developing country wishes to make improvements to a proprietary crop technology, the same patent jungle can make it difficult to transfer these improvements to farmers. "When you start having tens or hundreds of patents necessary to reduce to practice one idea, then it becomes untenable. And basically innovation grinds to a halt," especially for technologies that are not obviously profitable, says Richard Jefferson, CEO and chief scientist at CAMBIA, a non-profit research institution in Australia.

To help change this situation, Jefferson has created the Biological Innovation for Open Society (BIOS) Initiative [<http://www.bios.net>]. Similar to the open-source licensing approach currently transforming the computer software industry, the initiative is based on the idea of a protected commons: If a scientist makes a core improvement to a licensed technology, the community (which can include scientists from private and public sectors and developed and third-world countries) can have access to this improvement and can use it for commercial purposes. Scientists can initiate a project or join an ongoing one, as well as share information, through BioForge [<http://www.bioforge.net>], a Web-based meeting place for BIOS participants.

"Anyone can get free license to the technology, but they have to agree to put any improvements back into the licensing pool. So it leads to a kind of iterative collaborative research process in which the basic tool winds up getting improved," explains Gary Toenniessen of the Rockefeller Foundation, which partially funds BIOS.

**A CORE TECHNOLOGY** BioForge's flagship technology is Trans-Bacter, a new technique for gene transfer

to plants, which scientists developed at CAMBIA and described in February in *Nature*.<sup>1</sup> The technique is novel because it relies on bacterial species other than *Agrobacterium tumefaciens*, a commonly used gene-transfer tool covered by patents held by a number of large biotech companies including Syngenta and Monsanto.

In nature, *Agrobacterium* induces galls in plants by inserting a portion of a tumor-inducing (Ti) plasmid into a plant cell. This so-called transferred DNA (T-DNA) then integrates into the host genome. Agricultural scientists have exploited this mechanism, deleting oncogenes from the Ti plasmid and substituting transgenic genes that endow plants with the ability to resist herbicides or generate nutrients.

The CAMBIA team removed the T-DNA locus from a Ti plasmid isolated from a virulent strain of *Agrobacterium*. The researchers then introduced the T-DNA into three non-*Agrobacterium* strains, along with a novel plasmid containing a new T-DNA sequence, and GUSPlus, a new BIOS-licensed reporter gene that permits sensitive visualization of gene-transfer events. They found that each species could transfer genes to a variety of plant types, including tobacco, *Arabidopsis*, and rice, with varying levels of efficiency.

Steven Hughes of the Center for Genomics in Society at the University of Exeter, UK, notes that the CAMBIA research has implications for the understanding of horizontal gene-transfer events, as it demonstrates that several bacterial species can transfer genes to an organism outside their phylogenetic kingdom. "*Agrobacterium* was assumed to be the only organism with that potential," Hughes says.

More broadly, TransBacter was developed with the intent to fall outside the scope of existing patents. As the authors note, the majority of patents covering gene transfer to plants refer specifically to *Agrobacterium* as the transfer medium and not to the segment of DNA actually responsible for transferring the gene of interest. "By analyzing these patents, we found an Achilles' heel, which is that their definitions of the properties are restricted to the *tumefaciens* species or the *Agrobacterium* genus," says Jefferson, who notes that BIOS is not restricted to agriculture or even biotechnology but can be applied broadly to all types of biological innovation.

It's too early to know whether academia and industry will embrace the BIOS model. Plant geneticists in the public sector will likely be interested in the approach, says Steven Strauss, professor of forest science at Oregon State University in Corvallis. "We feel [that] unless there's something like an open-source alternative, we're just disenfranchised."

But, University of Arizona plant geneticist Richard Jorgensen notes that for many academics using proprietary technologies for research purposes, patents are not an issue because most large biotech companies don't enforce them in such cases. "The average scientist will probably have to be convinced; they may not jump at it," says Jorgensen. "But I would think anyone in a smaller company, smaller entities that don't want to be controlled by large ag-biotech companies, would be really enthusiastic about participating in something like this, because it's their ticket potentially to independence."

## References

1. W Broothaerts et al, "Gene transfer to plants by diverse species of bacteria," *Nature* 433: 583-4. Feb. 10, 2005

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