Ronald PC. Genetic Resource Recognition Fund. 1998. AgBiotech News and Information 10 (1): 19N-21N. CAB International.

Genetic Resources Recognition Fund

Pamela C. Ronald

Abstract

Crop germplasm from developing countries provides a major source of biological material for the development of improved crop varieties and medicines. Biotechnologists are increasingly cloning and patenting genes derived from these sources. Engineering and introduction of these genes into crop plants and other organisms is likely to lead to major advances in agriculture and medicine with potential worldwide benefits. Commercialization of these new products also brings concerns regarding who will benefit financially. While most recognize the importance of equitable sharing of benefits derived from genetic resources obtained from developing countries, few practical solutions have been implemented to achieve this goal. In a step towards recognizing the source nations and institutes that have contributed to making possible important scientific advances, the University of California at Davis has set up the Genetic Resources Recognition Fund (GRRF). Part of the royalties derived from the licensing of academic discoveries using developing countries' materials can be used to fund fellowships for developing nation scientists.

Biodiversity, genetic resources, and biotechnology

Plant biodiversity provides the genetic resources that are critical to the improvement of crops through biotechnology. Given the increasing worldwide demand for food, biotechnology, if used appropriately, has the potential to increase crop yields without the environmental hazards associated with pesticide and fertilizer use. Plant biodiversity also provides sources for new drugs such as anti-cancer medication and antibiotics. The value derived from biological diversity far exceeds the world investment in conservation (Brush, 1996).

In cases where biodiversity has been consciously conserved, the rewards have been great. An international system of gene banks has been established that conserves extensively collected germplasm for evaluation and use in breeding programs. For example the International Rice Research Institute Rice Germplasm Center preserves 83,0000 of the estimated 120,000 rice varieties (IRRI, 1990). The benefits to the world community from work at international centers has been "enormous, with low income food consumers in developing countries receiving the vast majority of those benefits. The total value of germplasm flowing through international research centers to industrialized countries benefited industrialized countries by not less than $3.5 billion annually while the benefits to developing countries for wheat and rice only were approximately $67 billion annually" (Jacoby and Weiss, 1997). While conservation and use of plant biodiversity has clearly benefited food production worldwide, a particular country where a specific crop genetic material originated may not have benefited directly.

There is growing concern that industrialized nations, who have the technology and resources to patent and develop commercial products, profit from biodiversity without compensating the providers of the source germplasm (Jacoby and Weiss, 1997). One of the difficulties in assessing appropriate compensation is in predicting that a particular gene will lead to a marketable product. In fact a particular genetic contribution usually represents only “a small percentage of the total value of the eventual product” (Jacoby and Weiss, 1997). In addition, the research and development process required to commercialize a particular product requires enormous technical knowledge, capital investment, financial resources, marketing efforts, distribution capacity, and time and is often beyond the budget of developing countries and Western universities (Jacoby and Weiss, 1997).

Patents are designed to reward those who make inventive and useful contributions to society. In a landmark decision, the U.S. Supreme Court ruled in 1980 (Diamond vs. Chakrabarty; 447 U.S. 303 (1980)) that a genetically engineered strain of bacteria that could break down crude oil was a proper subject matter for patent protection under the patent statute. Patenting is likely to continue to play an important role in shaping biotechnology as gene cloning becomes more routine. Whether the principle of patenting genes is morally or ethically correct is a matter of intense debate (Gladwell, 1995). On the one hand are those that see all biological material as belonging to God and therefore something that cannot be owned by an individual or company (Gladwell, 1995). On the other hand are those that see patents as a spur to the process of discovery and development of socially beneficial products and believe that the real ethical lapse would be “for geneticists, having conceived of technologies with vast and immediate therapeutic value, *not* to try to bring them to market as quickly as possible” (Gladwell, 1995)

Meanwhile, while the debate rages on, scientists are increasingly patenting valuable genetic discoveries and are working with private companies to develop the invention into a commercial product. This article focuses on a method to compensate developing countries' contributions while at the same time encouraging commercial development of potentially valuable crops for agriculture.

The Xa21 gene

Rice is the most important staple food in the developing world and improvements in rice yield have a significant impact on global food production. It is estimated that 50% of the potential yield of the world rice crop is lost to diseases caused by bacteria, fungi and viruses. One of the most serious bacterial diseases of rice in Africa and Asia is bacterial blight caused by *Xanthomonas oryzae pv. oryzae (Xoo*). Bacterial blight is one of the oldest recorded rice diseases and has been problematic for over a century. The discovery and cloning of the rice *Xa21* disease resistance gene which confers resistance to diverse *Xoo* isolates, provided a test case to develop a strategy for collaborative innovation and commercialization of new rice varieties as well as to develop a strategy for compensation.

In 1977, Dr. S. Devadath, of the Central Rice Research Institute in Cuttack, India, identified an individual of the wild species of rice, *O. longistaminata,* that was highly resistant to all tested isolates of the bacterial blight pathogen, *Xoo,* in India. *O, longistaminata* is an African perennial rice that is found as a weedy associate of cultivated rice in many areas. (Richards, 1996). The resistant *O. longistaminata* individual, which originated in Mali, was brought to the International Rice Research Institute (IRRI) in the Philippines for breeding studies in 1978 (Khush et al , 1991). Dr. G. Khush, Dr. R. Ikeda and coworkers at IRRI introduced the resistance into cultivated varieties using traditional plant breeding techniques (Khush et al., 1991). They found that the resistance was due to a single locus, called *Xa21*. Using material obtained from IRRI, P. Ronald mapped the locus in 1990, at Cornell University in the laboratory of S. Tanksley (Ronald et al., 1992). Dr. Tanksley's group had recently completed construction of a rice genetic map with support from The Rockefeller Foundation which had facilitated mapping efforts worldwide (McCouch et al., 1988). From 1992-1995 high resolution mapping, DNA library construction, cloning and sequencing was carried out at UC Davis leading to the isolation of a few candidate clones carrying *Xa21*. This work was supported by the USDA, NIH, and The Rockefeller Foundation.

A collaboration with Lili Chen at the International Laboratory for Tropical Agricultural Biology (ILTAB) in La Jolla, CA, co-directed by C. Fauquet and R. Beachy, was formed to transform a susceptible rice variety, Taipei 309 with the candidate *Xa21*-carrying clones. The resulting plants were assayed at UC Davis for bacterial blight resistance. One of the candidate clones conferred high levels of resistance to bacterial blight in transgenic plants. The coding region was located on the transformed piece of DNA and named *Xa21* (Song et al, 1995*)*. A patent application covering the *Xa21* sequence was filed in 1995.

Once cloned, there was tremendous international and commercial interest in using this gene to develop modern crop varieties. Species of *Xanthomonas* infect virtually all crop plants. Thus, in addition to improving crop production in rice, *Xa21* may be useful to develop new means of disease control in other crops such as the commercially important wheat, maize and barley. It is likely that without a patent application on file there would be less commercial interest and therefore less overall investment in developing the gene for use in these other crops. Ultimately, deployment of such engineered varieties could reduce the application of pesticides to the environment. Thus, the scientists were confronted with the question of how to develop further this technology for use in crop improvement programs as well as how to recognize source nations who had contributed to the initial breeding efforts.

The GRRF

Because there was no university precedent for germplasm compensation to source countries, and because there was no prior agreement governing intellectual property rights (the material was collected in Africa before the entry into force of the United Nations Convention on Biological Diversity), UC Davis wished to define an appropriate method of recognition to the germplasm source countries. The absence of some form of recognition was deemed inappropriate and would likely make it more difficult in the future for the university to obtain research access to developing nation genetic materials. Our goals were five fold: 1. To establish a mechanism to recognize and compensate for germplasm contributions from developing nations. 2. To provide a means for scientists to patent their inventions while maintaining productive collaborations and good relations with scientists from developing countries. 3. To encourage University/Developing nation/Industry links for commercialization of genetically engineered products. 4. To create a constructive solution that would be easy to implement and be widely accepted. 5. To create economic incentive for continued sharing of germplasm and conservation efforts.

At the suggestion of Professor John Barton of Stanford University, an expert in international genetic resources law and technology transfer, it was decided that a fund dedicated to advanced study would be an appropriate form of compensation because it was likely to be more beneficial to the source nations than a direct financial transfer insomuch as it is usually not possible to determine who in particular should receive compensation as the owner of a specific genetic resource. In June 1996, the University of California at Davis established the Genetics Resource Recognition Fund (GRRF) to recognize contributions of developing nations to the success of the *Xa21* cloning (see below). The GRRF will be funded from royalty income generated from commercialization of genetic materials derived from germplasm obtained from developing nations (eg. the rice gene *Xa21* was derived from material gathered in Mali). The GRRF will be used entirely for fellowship assistance to researchers from developing nations who will return to their country and work to ensure that the information they have learned will benefit others in their home country. Students from germplasm source countries (in this case, Mali) would have first priority.

The GRRF provides fellowships to scientists from the germplasm source country after the first year of commercialization. By providing a method to share potential benefits, the GRRF accommodates researchers and academics who wish to explore, develop, and collaborate with potential donors of germplasm. Although the GRRF makes no effort to assess the future potential income generated from the invention, it provides an efficient method and viable solution. The fund will benefit the individuals and farming communities from where genetic resources were obtained independent of the channeling of funds through international agricultural research centers or individuals. Finally, the fund provides a framework whereby commercial interests will be able to obtain samples and information at an equitable cost.

Because it is virtually impossible to predict the commercial success of a particular product, the GRRF will rely upon a flat fee. Currently the UC Davis fund has raised nearly $150,000 of future royalties from industry, UC Davis and inventors' contributions. As additional discoveries are made and licensed to industry, this amount should grow. Another option is that contributions could take the form of a percentage of the royalty income. Other forms of compensation like conservation or health care could also be incorporated into future agreements. It is inevitable that the total amount provided to developing countries by the GRRF will be judged to generous or too miserly depending on the perspective. My goal is to have all future agreements between UC and companies that license UC inventions specify a contribution to this fund if the material being licensed was derived directly or indirectly from a developing country. By depositing all the royalties in one fund, the risk that one license may not be profitable would not diminish the overall effectiveness of the fund. Thus each country that contributes genetic resources will benefit from this fund independent of the commercial success of its particular contribution.

Our goal was to create a practical compensation method to genetic resource contributors while allowing for the development, dissemination and commercialization of their contributions. The GRRF is a special fund set up for income derived from *Xa21*. However, it is hoped that the GRRF concept will be widely adapted by all the University of California campuses and in other major agricultural and medical research institutions. The setting up of similar funds at other major research institutions would provide a large and ongoing source of funds for fellowships or other types of contributions. The presence of compensation programs would encourage source countries to conserve valuable land and genetic resources and can provide an economic incentive to do so.

Non-commercial researchers, such as those in government funded programs, would continue to enjoy free access to the genes, so long as they do not develop commercial products based on that genetic material. For example UC Davis and IRRI have agreed that IRRI will have full rights to develop new rice cultivars using the cloned *Xa21* and freely distribute this material as well as the cloned gene to developing countries. If the lines perform as well as locally adapted varieties, national breeding programs will have full rights to distribute such lines to farmers in the developing world and need pay no royalties for this purpose. Because the gene is passed onto the progeny, farmers can grow their own seed for the next season. The new variety will be genetically identical to the locally adapted variety except for the addition of a single rice-derived gene conferring resistance to bacterial blight. Other traits important for local adaptation (such as drought resistance, cold tolerance, or short stature) are expected to remain unchanged. If issued, the *Xa21* patent does not preclude the use of *Xa21* by conventional breeding.

There is an ongoing need to protect the worlds genetic diversity and to ensure collaborations to use genetic resources to develop improved crop varieties both through traditional approaches and biotechnology. The alternative is “a deterioration in the world's ability to cope with the problems of hunger and disease” (Jacoby and Weiss, 1997).

A sample text is provided below that can be adapted to a particular institution for the purpose of setting up a GRRF.

In addition to other royalty obligations, company x shall annually pay n% of sales of products and derivatives of gene x as defined in Article X, into a genetic resources recognition fund for n years following the end of the first year of commercialization, until it has transferred a total of X$ into that fund under this agreement. The genetic resources recognition fund shall be maintained by the university as a separate restricted fund, to be used entirely for fellowships and fellowship assistance to students and postdoctoral researchers from developing nations studying agriculture with a preference to be given to students and researchers from (name of source countries). The GRRF shall be managed by the A Dean of the College of Agriculture and Environmental Science of the University of California at Davis.

Acknowledgments: Many thanks to R. Adamchak, J. Barton, K. Bastian, S. Brush, C. Jacoby, C. Qualset, R. Stanley, and G. Toenniessen for critical reading of the manuscript.

REFERENCES

Brush S. 1996. Whose knowledge, whose genes, whose rights? In Valuing local knowledge: Indigenous people and intellectual property rights. Pp. 1-21 Brush S and Stabinsky D, eds. Island Press, Washington DC.

IRRI Rice Facts, 1990.

Jacoby, CD and Weiss, C. 1997. Stanford Environmental Law Journal. Vol. 16,p. 74.

Gladwell M. 1995. Rights to Life: Are scientists wrong to patent genes? The New Yorker Nov. 13, pp. 120-124.

Khush GS, Bacalangco E, Ogawa T (1991) A new gene for resistance to bacterial blight from *O. longistaminata.* Rice Genet Newsletter 7:121-122.

McCouch SR, Kochert G, Yu ZH, Wang ZY, Khush GS, Coffman WR, Tanksley SD (1988) Molecular mapping of rice chromosomes. Theor. Appl. Genet. 76:815-829

Richards P, 1996. Culture and community values in the selection and maintenance of African rice. In Valuing local knowledge: Indigenous people and intellectual property rights, Brush S and Stabinsky D, eds. pp. 209-229. Island Press, Washington DC.

Ronald PC, Albano B, Tabien R, Abenes L, Wu K, McCouch S, Tanksley S. 1992. Genetic and physical analysis of the rice bacterial blight resistance locus, *Xa21*. Mol. Gen. Genet. 236:113-120.

Song W-Y, Wang G-L, Chen L, Kim H-S, Pi Li-Ya, Gardner J, Wang B, Holsten T, Zhai W-X, Zhu L- H, Fauquet C, Ronald P. 1995. A receptor kinase-like protein encoded by the rice disease resistance gene *Xa21*. Science, 270:1804-1806.