

A Comparison of the Plant Genome and Human Genome Projects

Editor's Note: The Human Genome project and the sequencing of the genes therein has created a most deserving spot in our history. Scientifically, the human genome project is already revolutionizing our understanding of sporadic and inherited diseases, including cancer, Alzheimer's, autism, and many more. It can be argued that the first drugs designed on the basis of gene discovery were inhibitors of the novel protease found in the genome of HIV, drugs which have radically improved the prognosis for AIDS. Now that the genomes of microbes and viruses are known, as well as their human hosts, drugs that uniquely target pathogens will follow this example in large numbers. Much of the debate over crop plant genomics echoes the debate surrounding the human genome project 20 years ago. While the model plant genomes have transformed basic plant biology in much the same way as animal genomes have, there are major differences between crop plant genomics and the human genome project.

At the outset of the human genome project in the mid-1980s, there was heated debate over the merits of a project scheduled to take 15 to 20 years and to cost in excess of \$300 million. Arguments against the enormous undertaking ranged from scientific, to economic, ethical, and educational. It was argued that conventional biomedical research would have to be abandoned to fund the project; that graduate education would take a back seat as students were trained in sequencing and little else; and that the sequence of our genes would breach our inalienable right to privacy. Finally, there was an underlying conviction that the human genome sequence would be of little scientific value compared to the outrageous cost.

In actuality, the human genome project was completed in less than 10 years, and cost the U.S. taxpayer less than \$500 million. Technological advances halved the anticipated costs year after year, following "Moore's Law," which predicted comparable increases in computer speed and memory over the same time period. It is projected that, by the end of this decade, an entire human genome will cost less than \$10,000 to sequence.

Plant Genome Sequencing

What lessons are there to be learned from this experience for crop plant genomics and plant breeding? As with animals, model genomes (nematode, fly) have been sequenced first (*Arabidopsis* and rice, *Oryza sativa* L.). However, now that they have been completed and their impact is being felt in basic research, should we go on and sequence major crops such as maize (*Zea mays* L.), soybean [*Glycine max* (L.) Merr.], wheat (*Triticum aestivum* L.), cotton (*Gossypium* spp.), and trees?

Much of the debate over crop plant genomics echoes the debate surrounding the human genome project 20 years ago. However, there are major differences between crop plant genomics and the human genome project. For one thing, human genome research contributes to biomedical research and development, a \$1 trillion activity worldwide. Crop plant genome research also underlies enormously important industries in food, feed, energy, and fiber,

but here the analogy ends. First, several species must be targeted to cover agriculturally important plants, rather than one genome in the case of biomedical research. Second, the seed industry operates on far lower margins than the pharmaceutical industry, and has raised public concerns over food safety and security. Finally, the genetic information available to plant breeders is usually thought to be far less extensive than the vast array of epidemiological data collected by the biomedical community, making the sequence less useful.

With respect to sequencing technology, plant genomes pose problems because of their size and repetitive content, as well as the number of different species required. This issue has been addressed by taking advantage of the observation that most methylation in plant genomes is restricted to transposons and high copy repeats. By sequencing only the unmethylated portion of the genome, or by subtracting repeats, costs can drop by 10 fold or more, making the sequence of multiple large genomes practical.

What Is Value of Plant Genome Sequencing?

The value of the collective knowledge gathered by plant breeding has been underestimated, in part because of controlled pedigrees which are unavailable in human populations. Once genes underlying individual traits are known, the basis for disease resistance and stress tolerance is likely to emerge as it has in model organisms, allowing more precise "diagnosis" in breeding programs as well as genetic modification. The sequence can also be used to detect epigenetic, as well as genetic variation which likely contributes to traits such as flowering time, perennialism, apomixis, and heterotic performance. New pesticides and herbicides will also emerge from comparative genomics of crops and their pests, just as new antiviral and antimicrobial drugs are emerging in the pharmaceutical industry by selecting pathogen targets that are not found in the human genome and are less likely to be toxic. The HIV protease is one example of such a target, and protease inhibitors are some of the most successful antiviral drugs ever introduced.

Finally, the economic value of agriculture to a growing world population must not be underestimated. While the pharmaceutical industry is successful because of aging western populations, agriculture is the priority for crowded, youthful, hungry nations that make up the rest of the world. The imperative to modernize agricultural research is becoming clear.

Thus genomics can provide a road-map for the next generation of agricultural and breeding research, but it cannot replace the geneticist or the plant breeder. What it can do is open new areas of research unimagined by conventional plant breeding. Imagine, for example, small, nontoxic molecules that delay flowering or trigger apomixis. Given the importance of agricultural research for food security, energy conservation, and the environment, as well as the rich genetic resources available, genomics may yet make a greater impact on plant breeding than the human genome has had in biomedical research.

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