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# The Biotech Frontier

**William Haseltine explains the medical, energy, and industrial implications of the genomic revolution.**

**William Haseltine**

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Rice grown in culture. Photo by International Rice Research Institute (CC).

*EXCERPT: When most people think of the Human Genome Project, they think of it as a new knowledge base with the potential to transform modern medicine. But the effects of genomic research are much broader, with equally immense implications for the global economy and our natural environment. Ann Graham talks with biotech innovator* ***William Haseltine*** *for strategy+business magazine.*

**Where are the most important advances in genomics emerging?**

The major benefit of genomic science thus far has been for humans. But in the long run, it is not just *for* humans. It is *of* humans. Through the genomic revolution we are opening up all the genomes of life for our perusal, and few people have thought through the implications.

Medicine will still be important going forward; every week brings a few new genomes into our knowledge banks. But I don't think medical applications will be the major use for investment dollars. The next revolution is going to be about energy, agriculture, and materials science. That, I think, is going to surprise people. Most of life on Earth is invisible. From the bottom of the sea at the hot sea vents, to the dirt under our city streets, there's an enormous range of microorganisms that play fundamental roles in shaping the course of life everywhere. Now, genetic science allows researchers to intervene at that level.

If you think about the future of biotechnology, what's old is becoming new again.

**What do you mean by that?**

*Biotechnology* literally means technology applied to manipulate the living world. Humans have been at this a very long time. It's one of the oldest technologies, and its greatest successes have been in agriculture, animal husbandry, and fermentation.

Now we are back in the same arenas, with a new set of emerging technologies. To give you an idea of the excitement around the use of biotechnology for energy: The Berkeley Center for Synthetic Biology received about $1 billion in grants in 2007. I'm the chairman of the board of trustees of this group. It was founded and is directed by Jay Keasling, a professor of bio- and chemical engineering at Berkeley and the director of Lawrence Berkeley National Laboratory's Physical Biosciences Division. About half the energy research money came from BP and the other half came from federal grants. This is only the beginning. Biotechnology will be the basis for a whole new petroleum-free carbon-based economy.

CARBON-NEUTRAL ENERGY FARMS

**How would synthetic biology produce energy on a mass scale?**

*Synthetic biology* is not a name I like. I prefer to call this new discipline *constructive biology*, because this form of biology constructs new molecules.

But to answer your question: Plants have been fixing carbon from the atmosphere with the energy of sunlight, and converting it to fossil fuel, over the course of several hundred million years. This means that living systems have the power, of course, to make our fuel. The trick is to do it much, much faster.

We already know how to effectively create biomass from plants. We grow forests for wood; we have agriculture. With a combination of modern biotechnology techniques we could remove carbon from the air, turn it into a fuel, use that fuel, and return the carbon to the atmosphere so the whole process is carbon-neutral with respect to the concentration of carbon dioxide in the atmosphere. Essentially, these techniques would allow us to farm energy, coupling the photosynthetic process with biochemical production of useful hydrocarbons.

Let me take you back in time to think about that for a minute. Before there was life on Earth, it was basically a wet, hot rock. When it cooled down, it was a rock with water. Living organisms arose (we're not quite sure how), and over the course of several billion years, they transformed rock and water into this beautiful Earth. That's enormous chemical power, and all of it is locked up in the genes of organisms that proliferate all over the world.

Now that we can directly read genomes, store them in computers, and analyze them, and splice genes from one organism to another, we can move hydrocarbons through almost any chemical pathway we want. Suppose you wanted to take yeast that normally makes ethanol and convert it to yeast that makes diesel fuel. You would write up the chemical path to show the normal process to ethanol, and then reroute the path to diesel fuel. In modern organic chemistry, that would involve a series of eight or nine steps in a test tube using various catalysts. But now you can use genome database analysis to identify and isolate enzymes that can provide that pathway naturally. You can then modify those enzymes so they're more efficient. This is an example of constructive biology.

We know constructive biology works because these were the methods used to produce the antimalarial drug artemisinin in both bacteria and yeast. Plants use a very complicated and expensive process to make artemisinin. At the Center for Synthetic Biology, a project led by Jay Keasling (and funded by the Bill and Melinda Gates Foundation) re-created the entire pathway both in bacteria and in yeast. That breakthrough, which makes artemisinin cheaper to produce and therefore affordable to the world's poorest children, has made Keasling a leader in the field of constructive biology.

**You mentioned energy farming. What does that look like?**

Many microorganisms grow in the sea, and there are a number of potential ways to use them for energy production. One is to place algae tanks far below the surface, but not so deep that they can't get sunlight piped down to them. Another is to create a series of saltwater-filled tubes on the surface of a large desert and place algae so that sunlight is absorbed as you pump the water through. There are a number of places in the world where huge deserts are right next to the sea. You don't want to use arable land, and this gets us away from freshwater, too.

These farms could create a continual atmospheric carbon-neutral production cycle: algae taking sunlight, fixing carbon, and producing useful fuels. As I said earlier, what is old is new again. Humanity used to burn wood for energy. Less than 200 years ago, we started burning fossil fuels. Now we're returning to the older process, but it's more efficient with the modern advances of genomics, gene regulation, gene splicing, microbial cultivation, and massive ocean engineering.

**Doesn't that suggest a reorientation for the energy industry?**

Some oil companies are already calling themselves energy companies. In the future, energy companies will be diversified. They will primarily use solar and wind energy to produce electricity and fuel; they will also provide some fossil fuel energy and atomic energy. The materials sector is also very important; it will be the next focus of synthetic biology and of chemistry. All the chemical companies are very interested in petroleum substitution and micro-materials, and the life sciences have enormous amounts to contribute to material manufacturing as well.

MICROBIAL MANUFACTURING

**How will basic industrial manufacturing processes be changed?**

New manufacturing processes will not use the vats typical of a chemical plant. Instead, the manufacturing basis for materials will be microbial. Life sciences teach us that if you have one good organic substance, it can reproduce itself endlessly and reproduce those products. All you have to do is keep feeding it. You don't have to keep making it again and again and again. We already know how to produce plastic precursors with yeast and bacteria or plants. So we can grow these materials as we manufacture them.

**What is the connection between nanotechnology and biotechnology?**

The fundamental architecture of matter is an atom and a molecule. Something as large as a forest is made of very tiny substances, hooked together. Life and materials sciences are teaching us that we can arrange atoms in precise locations, to self-assemble and form units in small to very large sizes—replicating the manufacturing processes of nature. The fact that forests grow and that bacteria proliferate shows you that nano-machines work, and can be very efficient. We can build materials that self-assemble, and this means we can reduce the amount of material used in our lives. For example, we don't have to carve objects out of great masses of metal (and discard the waste), because we can have them assembled, at the molecular or multimolecular level, with every molecule used. Eventually we can make them intelligent so they'll assemble on command. The basic unit would be a very tiny, submicroscopic unit embodied with the information that says, "connect A, B, C, D." It will then, in effect, construct itself: We can make a chair, we can make a table, and we can build a house.

This type of construction will probably not be available until the end of this century or the beginning of the next century. Think of it as an intelligent Lego set that you could program so the pieces compose themselves. You could then create a program that says, "Make a candlestick, make a chair, and make a wall." Ray Kurzweil describes these types of technologies in his book *The Age of Intelligent Machines* (MIT Press, 1992).

**What are the implications for food production?**

Earth's population is projected to rise to almost 10 billion by 2050. So the need for freshwater and land is acute; we must use our agricultural land more intensively. Genetically modified organisms can help with that. They can produce higher yields and more nutritious foods. They can obviate the need for plowing. Most people don't understand what plowing is for. It's really just a weed control technology. You plow over and under the previous year's crop. But if you have the right combinations of environment-friendly herbicides and the agricultural crops that are resistant to those herbicides, you don't need to plow. No-plow agriculture saves topsoil and energy. Once you don't need so much nitrogen fertilizer or complex pesticides, you can get to an agriculture that is much more energy efficient. You can also breed in drought resistance.

People will be healthier as a result. And it will allow us to restore many habitats, because we'll be using less land to grow food.

**What about the fears about genetically modified foods?**

The technology is rapidly spreading, despite the European opposition. It's spreading in many parts of the world because of its obvious advantages. For example, meat is a highly inefficient source of protein; over the next 20 to 30 years, people will move from meat to plants as a source of protein. I've been in Chinese restaurants that serve something that looks like a fish with skin and scales, but it's entirely made out of soy protein, which is a plant product. You see a chicken that looks like a chicken, it's carved like a chicken, but it's not a chicken. You can make foods look and taste very attractive with manipulation, which, in this case, involves a process to spin soy proteins into fibers.

REGENERATIVE MEDICINE

**Most people, of course, still think of biotech as medical innovation. In that light, what is the significance of personalized medicine?**

In my mind, medicine has always been personal, if practiced properly. You are sick and a doctor interacts with you as an individual. This is one of the only times in your life when you have a professional response fully tailored to you as an individual. A good doctor wants to know about you and only you. Maybe he wants to know something about your family members, but that's because of their relationship to you. If medicine isn't personal, and isn't therefore personalized, then it's not really useful.

When people talk about personalized medicine they tend to focus on genetic inheritance, because it is fascinating to peer into your genetic past and present. But modern genetics, at best, is like looking at your future through a glass darkly. With very few exceptions, such as Huntington's disease, you can't say that if you have an inherited trait you'll get the related disease. In most cases, you have a probability between 10 percent and 0.1 percent of getting the disease; you don't know when or even if the disease will appear.

Ninety percent of breast cancer seems to have nothing to do with inherited genes. The same is true of prostate cancer in men. There is some role for genetics in predictive medicine, but it's a much smaller role than people think.

I believe the whole field of what's called genetic medicine is not really ready for prime time, if it will ever be ready. If I seem negative, it isn't because I think genetics is unimportant. It is just that genetic inheritance is a very minor aspect of genomics, whereas the applications that I've already outlined—energy, agriculture, and materials—are here and important now.

However, there is one tremendous breakthrough that I consider the ultimate personalization of medicine—using your cells to build new, healthier organs. Regenerative medicine involves developing your body's own replacement organs and tissues if they are lopped off, damaged, broken, or diseased. Combine that with materials science and you begin to build organs. I just was visiting Dr. Anthony Atala at the Wake Forest Institute for Regenerative Medicine. He leads an organization that is building new human organs. These are not artificial organs; they are made of your own cells.

It's going to be possible to build a new pancreas for a person who is a diabetic. We will be able to regrow a retina, a heart muscle, and eventually even an entire heart. This is happening because, through genomics, we understand what a cell is doing, we can move genes in and out of cells, and now we have the ability to move genes around the body.

Another, more immediate benefit is differential diagnosis. Because we can define most of the things a cell does, we can define the characteristics of diseases much more precisely. For example, we used to look at leukemia as one type of white-cell disorder, but it turns out that there are perhaps 20 different leukemia diseases. Each will take a different course; each will require a different treatment.

Modern biology has also given doctors more techniques for understanding the disease you have in its current state. Your genes can tell you what you inherited, but they can't tell you how your cells are behaving now. If you think about a lot of cancer tests, they're not about what you inherited. They're about what your cancer is doing today.

**What can you say about the progress of using genomics to create new drugs?**

There is no question that our knowledge has been helpful. But the problem also turned out to be much more complicated than anybody thought. People thought, for example, that maybe they would find a few extra genes that were involved in cancer. It turns out that almost every gene is involved in cancer at some level. And every cancer is genetically different. Even every cell in the cancer is different from every other cell. And maybe 20 or 30 major pathways are involved. Does gene research help us understand and solve cancer? Maybe it will give us some additional insights. But it isn't the answer to cancer.

BENEFITS FOR THE WORLD'S POOREST

**Can we expect the next wave of medical and green genomics to reach more of the two-thirds of the world's people who live at the "bottom of the pyramid," in lower-income countries?**

When the Soviet Union fell and the Cold War ended, the Russians, the Chinese, and the Indians all joined the global economy. C. K. Prahalad's *The Fortune at the Bottom of the Pyramid: Eradicating Poverty through Profits* [Wharton School Publishing, 2004] was one of the first books to recognize this. It is a profound work that is now changing the thinking of a new generation of leaders. What is about to happen, and is already happening in India, is a reorientation of business toward the 2 billion people worldwide who are emerging from poverty. This is a fundamental transformation.

**And it's not just about selling consumer goods to them.**

Absolutely not. The rest of the world is going to want energy, more food and better food, and good medicine. The structures that we currently have in place cannot deliver all of those things to so many people without destroying our world.

That's why we have to get away from petroleum-based energy. Agriculture needs to be much more efficient. We need to feed more people and to feed them well. Many solutions lie in biotechnology. It takes twice as much water, and I think about five times as much energy, to feed a meat eater as it does to feed a vegetarian. There is a tremendous savings to be had in promoting a vegetarian diet, and I think the world will move in that direction.

I am working in India now through a foundation I've created to deliver high-quality, cost-efficient health care. I believe it's possible to get equal quality at a cost between 10 and 20 percent below current costs. (See "The Innovation Sandbox," by C. K. Prahalad, *s+b*, Autumn 2006.) There are a number of experimental enterprises using technology to create high-quality, affordable, low-cost health care for the Indian middle and lower-middle classes. These are self-sustaining, profitable organizations. There is a tremendous amount of experimentation. The common theme is, How do you solve the problems of getting high-quality health care at very low cost to very large numbers of people?

That is not just a problem for health; it's a problem for the whole economy. How do you provide efficient energy, health care, food, and services to very large numbers of people? India is a great laboratory, because of its demographics and mix of high-tech wealth and poverty. And hopefully those solutions then get translated to another 2 billion people globally.

**Are you saying that the innovations spawned by biotechnologies can help eliminate the "have" and "have-not" economic extremes?**

You'll never see an end to economic disparity, but you will see unprecedented upward mobility in the developing world. We are already seeing something like 35 million to 40 million people a year moving into India's and China's middle classes. Think of it as a quarter of the United States' total population joining the middle class each year. Remember, it was middle- to lower-middle-income Americans, not the upper class, that drove the world economy until very recently.

Mass markets are very powerful, even when the price points are low. So we're seeing these huge transformations take place, and I think that they can continue, but we need to solve the production problems in order to make these lifestyles sustainable on our planet.

**Can industrial society be sustainable when there are nearly 10 billion people on the planet?**

Yes, if we replace our current generation of wasteful technologies. Biotechnologies will have a significant role in that change. If you look at the full range of what we've talked about, we have gone from burning wood to regrowing arteries. That's a pretty broad span of life sciences, and it's tremendously exciting.

*Ann Graham is is a contributing editor of* strategy+business*. She is the coauthor, with Larry Rosenberger and John Nash, of* The Deciding Factor: The Power of Analytics to Make Every Decision a Winner *(Jossey-Bass, 2009).*