DOE/SC-0104

U.S. DEPARTMENT OF ENERGY'S

Bioenergy Research Centers

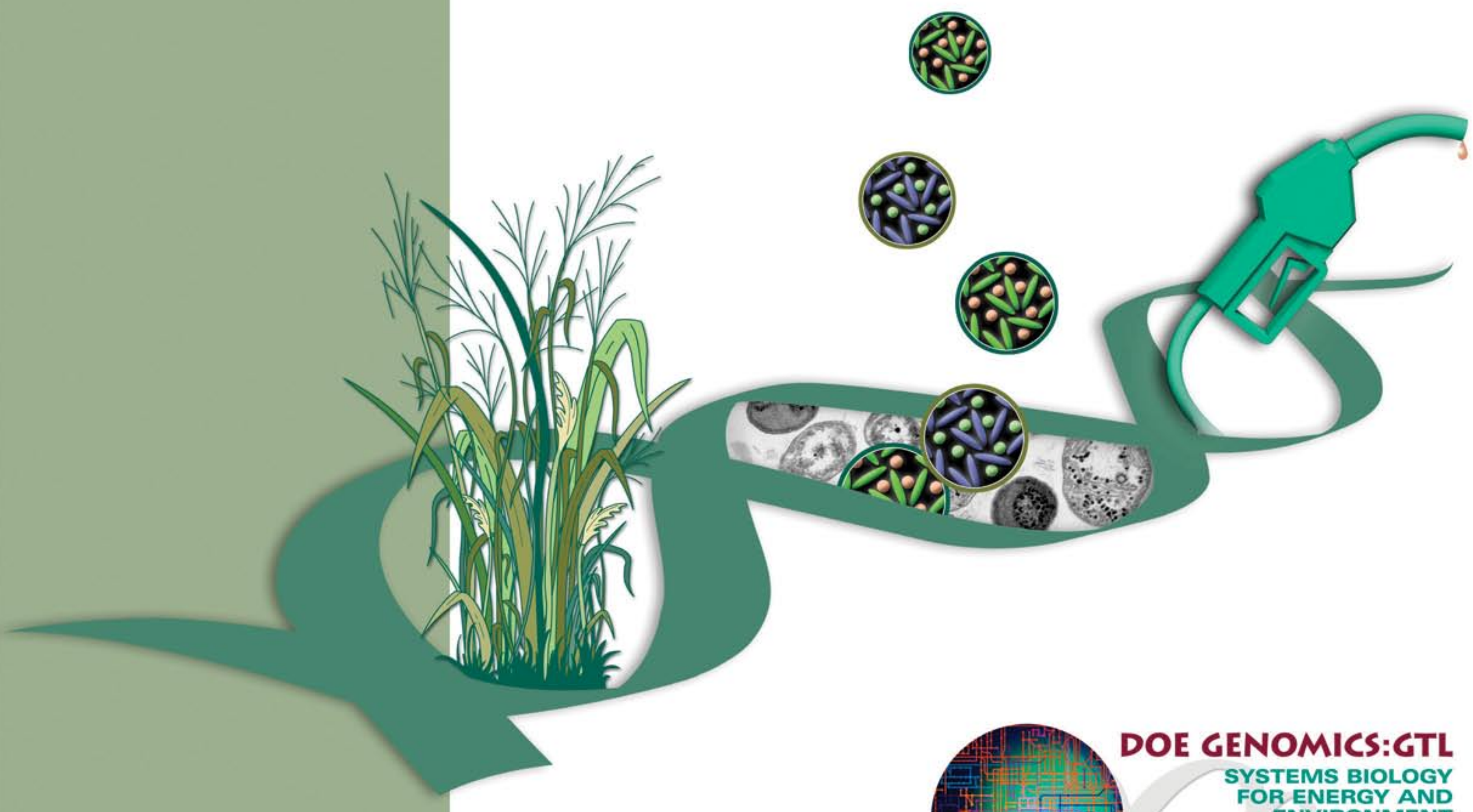
An Overview of the Science

U.S. DEPARTMENT OF ENERGY

Office of Science

Office of Biological and Environmental Research

DOE Bioenergy Research Centers

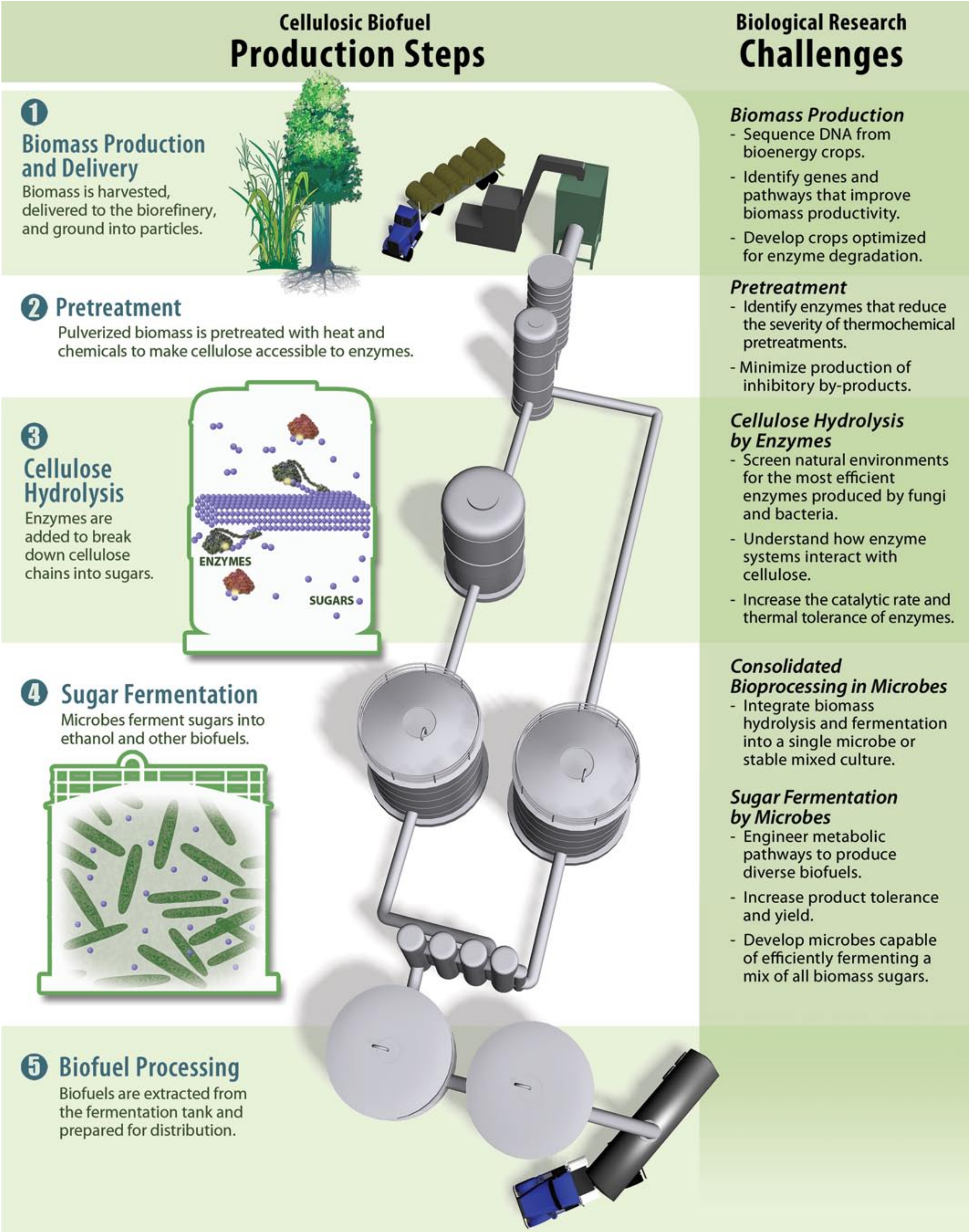


February 2008

DOE GENOMICS:GTL

SYSTEMS BIOLOGY FOR ENERGY AND ENVIRONMENT

OFFICE OF SCIENCE
U.S. DEPARTMENT OF ENERGY



Cellulosic Biofuel Production Steps and Biological Research Challenges. This figure depicts some key processing steps in an artist's conception of a future large-scale facility for transforming cellulosic biomass (plant fibers) into biofuels. Three areas where focused biological research can lead to much lower costs and increased productivity include developing crops dedicated to biofuel production (see step 1), engineering enzymes that deconstruct cellulosic biomass (see steps 2 and 3), and engineering microbes and developing new microbial enzyme systems for industrial-scale conversion of biomass sugars into ethanol and other biofuels or bioproducts (see step 4). Biological research challenges associated with each production step are summarized in the right portion of the figure.

A Message from the Secretary of Energy

Greetings,

To build an energy secure future, we must trust in the creative genius of American scientists and engineers and empower them to pioneer the next generation of renewable fuels. In January 2007, the President set forth his Twenty in Ten plan, which called for the nation to reduce projected gasoline consumption by 20 percent by 2017. In December 2007, Congress responded and the President signed the Energy Independence and Security Act of 2007, which aims to improve vehicle fuel economy and sets a Renewable Fuel Standard of 36 billion gallons of biofuels by 2022.

To meet these goals, we need to continue to utilize clean, cutting-edge technologies that capitalize on breakthrough research and development. Technological advances in energy supply, distribution, and utilization will help ensure we meet the energy challenges of the 21st century and maintain our competitive edge.

As part of this effort, the Department of Energy is committed to addressing the fundamental scientific challenges that the creation of clean, renewable, cost-effective biofuels represents. In my view, advanced biofuels offer tremendous promise for helping our nation bring about a clean, safe, reliable, and affordable energy future.

With the establishment of the Department of Energy's three Bioenergy Research Centers described in this publication, in addition to other small and commercial-scale biorefinery projects the Department is pursuing across the country, we are taking essential steps to meet the goal of making cellulosic ethanol cost-competitive with traditional sources of energy by 2012.

These DOE Bioenergy Research Centers—the Bioenergy Science Center, led by the Department's Oak Ridge National Laboratory; the Great Lakes Bioenergy Research Center, led by the University of Wisconsin–Madison in partnership with Michigan State University; and the Joint Bioenergy Institute, led by DOE's Lawrence Berkeley National Laboratory—are now up and running and will advance basic scientific research and development necessary to help transform our energy future.

In my opinion, these centers may be among the most important projects we undertake during my time as Secretary of Energy. We know how to make ethanol from corn, and this country produced about 6 billion gallons of corn-based ethanol for fuel last year. But for biofuels to make a serious impact in the future without affecting the food supply and without adding to net greenhouse gas emissions, we need to learn to make biofuels cost-effectively from plant fiber, or cellulose. Cellulosic biofuels could substantially reduce U.S. oil consumption, help cut overall greenhouse gas emissions, and usher in a new green economy across the nation, one where family farmers embrace bioenergy feedstocks as a new cash crop.

The important work taking place at these Centers—making production of biofuels more efficient, less costly and commercially viable—may change the way we think about biotechnology and transform how we power this nation.

Sincerely,

Samuel W. Bodman
Secretary
U.S. Department of Energy

A Message from the DOE Under Secretary for Science

Dear Colleagues,

Energy and environment are the great challenges facing humanity today. According to the International Energy Agency, global demand for energy is expected to grow by more than 50 percent by 2030. Fossil fuel use will account for more than 80 percent of this increase. Increased consumption of fossil fuels will steadily grow emissions of carbon dioxide, augmenting greenhouse gases in the atmosphere. Thus, energy and the environment are inextricably linked. Reducing dependence on fossil fuels and imported oil is a challenge of vital importance to national security, the economy, and the environment.

The imperative of developing new, carbon-neutral forms of energy has never been clearer or more compelling. At its heart, the challenge is a scientific one. Substantial reductions in fossil fuel consumption will require more than incremental improvements in our current technologies; it will require *transformational* discoveries and breakthroughs in basic science that fundamentally change the rules of the game.

That is the mission of the three DOE Bioenergy Research Centers described in this publication. These three Centers bring together top scientists and researchers from multiple disciplines in the quest for the breakthroughs in basic science that will make production of biofuels cost-effective and commercially viable on a national scale.

Among the major options for reducing our nation's dependence on fossil fuels and imported oil, biofuels rank among the most promising. Biofuels produced from biomass, such as cellulosic ethanol, could replace perhaps as much as a third of the current U.S. demand for transportation fuels with a homegrown, renewable energy source without affecting food production. In addition, biofuels offer a major answer to both pollution and greenhouse gases: They burn more cleanly and are essentially carbon neutral (plants that are grown as biofuel feedstocks reabsorb the carbon dioxide emitted when the biofuels are burned).

The development of commercially viable processes for the conversion of cellulose or plant fiber into fuel poses technological challenges that have not yet been solved. Fortunately, over the past decades, we have made enormous strides in biotechnology and, in particular, in genomics-based systems biology. DOE, as the originator of the Human Genome Project and later a major partner, has pioneered many of the major advances and developed many of the new tools of this biotech revolution: High-throughput genome sequencing, high-intensity light sources for the imaging of life at molecular scales, and a variety of other state-of-the-art instruments that enable scientists to understand and reengineer biology at the system, cellular, and molecular levels. The Office of Science's Genomics:GTL program, as the heir to the Human Genome Project, has continued to pursue these discoveries, probing the plant and microbial world for innovative biotech solutions to the Department's missions in energy, carbon capture, and environmental cleanup.

The three Centers are designed to accelerate this effort in the vital area of bioenergy. The teams that lead these Centers are truly extraordinary. All three are multi-researcher, multi-disciplinary, multi-institutional partnerships, drawing on top talent from across the nation. While selected strictly on the basis of scientific merit, they benefit from being sited in geographically diverse locales. The BioEnergy Science Center is led by Oak Ridge National Laboratory, long a beacon of science and innovation in America's Southeast. The Great Lakes Bioenergy Research Center, led by the University of Wisconsin–Madison in partnership with Michigan State University, lies in the heart of the nation's Midwest breadbasket. And the Joint BioEnergy Institute, led by Lawrence Berkeley National Laboratory, benefits from its location in the San Francisco Bay area, a crucible of the biotech revolution and a leading center today for "green" investment and innovation.

While all three Centers are utilizing the powerful new tools of modern systems biology, their scientific programs are distinct, complementary, and mutually synergistic, as this document shows. They are attacking the barriers to cost-effective biofuels on multiple fronts, with the clear mission goal of developing usable knowledge that will advance biotechnology-based strategies for biofuel production, ultimately leading to technologies deployable in the nation's energy economy.

With this publication, we hope you can sense the excitement of this scientific endeavor, as the DOE Bioenergy Research Centers aggressively pursue breakthrough discoveries that promise to transform both science and energy security for our nation.

Sincerely,

Raymond L. Orbach

Raymond L. Orbach
Under Secretary for Science
U.S. Department of Energy

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URL for this Document

genomicsgtl.energy.gov/centers/brcbrochure.pdf

DOE Bioenergy Research Centers

Introduction

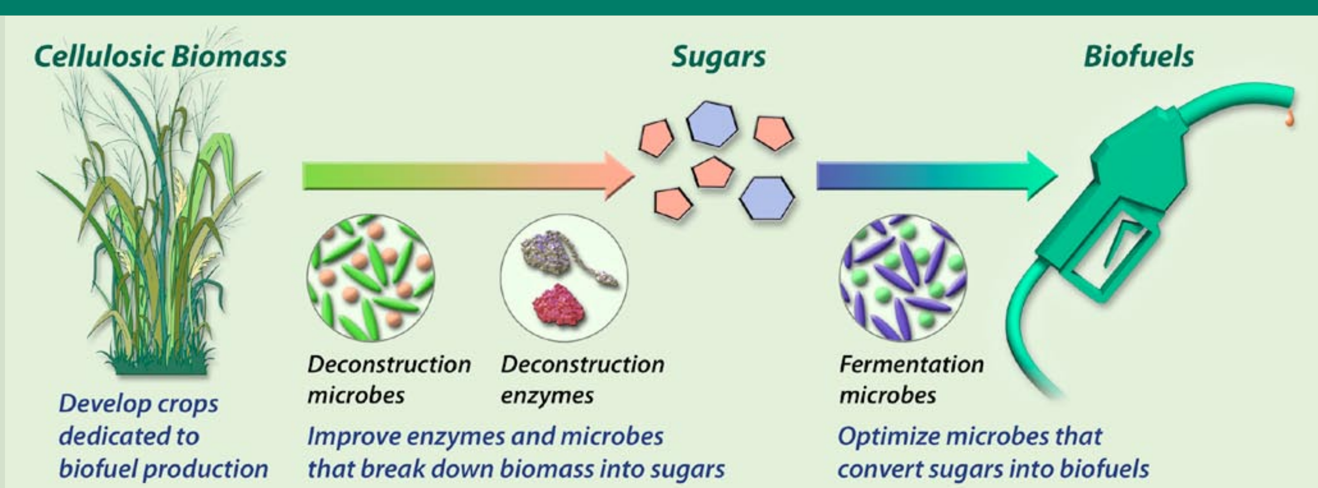
Alternative fuels from renewable cellulosic biomass—plant stalks, trunks, stems, and leaves—aim to significantly reduce U.S. dependence on imported oil while enhancing national energy security and decreasing the environmental impacts of energy use. President Bush's 2007 Twenty in Ten Initiative called for reducing U.S. gasoline consumption 20 percent over the next 10 years by improving motor vehicle efficiency and increasing the supply of diverse, less-polluting alternatives to petroleum. Congress responded to this, and in December 2007, the President signed the Energy Independence and Security Act, which will improve vehicle fuel economy and reduce U.S. dependence on foreign oil by increasing the use of biofuels. Ethanol and other biofuels from cellulosic biomass are renewable alternatives that could increase domestic production of transportation fuels, revitalize rural economies, and reduce carbon dioxide and pollutant emissions.

Although cellulosic ethanol production has been demonstrated on a pilot scale, attaining a cost-effective, commercial-scale cellulosic biofuel industry will require transformational science that can significantly streamline current production processes. This will further the Administration's considerable investments in biofuel research and development; as part of President Bush's goal to increase the use of biofuels, the U.S. Department of Energy (DOE) is on track to make cellulosic ethanol cost-competitive by 2012. Woodchips, grasses, cornstalks, and other cellulosic biomass are widely abundant but more difficult to break down into sugars than corn grain—the primary source of U.S. fuel ethanol production today. Biological research is key to accelerating the deconstruction of cellulosic biomass into sugars that can be converted to biofuels (see illustration on inside front cover, Cellulosic Biofuel Production Steps and Biological Research Challenges; figure below, From Biomass to Biofuels; and sidebar, Plant Cell-Wall Recalcitrance, p. 8).

The DOE Office of Science has played a major role in inspiring, supporting, and guiding the biotechnology revolution over the last 25 years. Building on advances in DNA technologies resulting from the DOE-initiated Human Genome Project, the DOE Genomics:GTL (GTL) systems biology program is creating a new generation of biological research. GTL is bringing together scientists in diverse fields to understand the complex biology underlying solutions to DOE missions in energy production, environmental remediation, and climate change mitigation. New interdisciplinary research communities are being created, as are knowledgebases and scientific and computational resources critical to advancing large-scale, genome-based biology. For more information on GTL, see p. 22.

To focus the most advanced biotechnology-based resources arising from GTL on the biological challenges of biofuel production, Energy Secretary Samuel W. Bodman announced in June 2007 the establishment of three new Bioenergy Research Centers (BRCs). Each center is projected to receive $135 million over the next 5 years, subject to funding from Congress, to pursue the basic research underlying a range of high-risk, high-return biological solutions for bioenergy applications. New scientific knowledge generated by the DOE BRCs will help lay the foundation for biobased products, methods, and tools that the emerging biofuel industry can use. The scien-

From Biomass to Biofuels



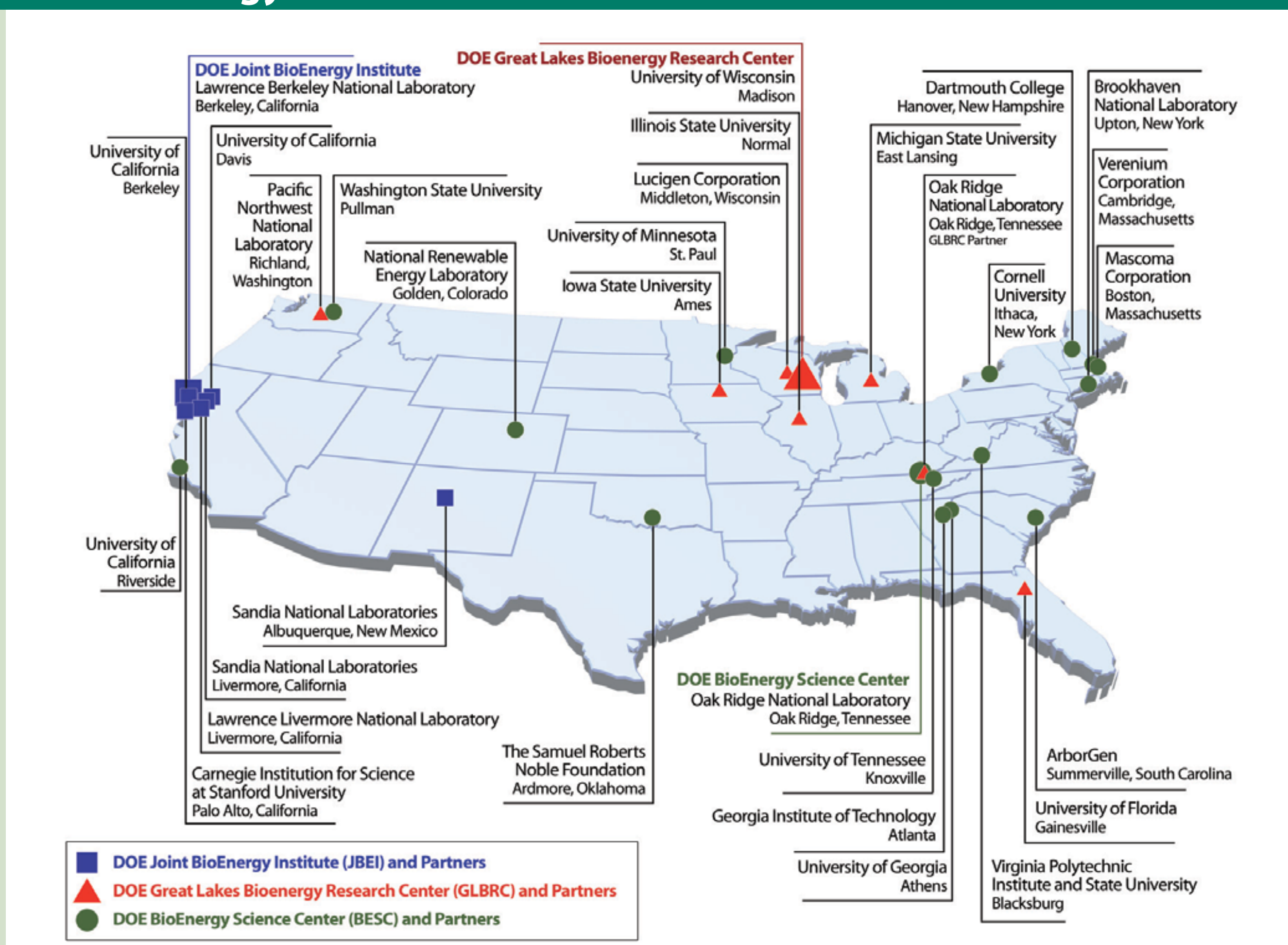
tific basis for these centers and for other fundamental GTL research critical to the biofuel industry was established at a DOE workshop involving members of the research community (see sidebar, Biofuel Research Plan, this page).

The three centers are based in geographically diverse locations—one in the Southeast, one in the Midwest, and one on the West Coast—with partners across the nation (see U.S. map, DOE Bioenergy Research Centers and Partners, below). A peer-review process was used to select DOE's Oak Ridge National Laboratory to lead the DOE BioEnergy Science Center (BESC) in Tennessee; University of Wisconsin–Madison to lead the DOE Great Lakes Bioenergy Research Center (GLBRC); and DOE's Lawrence Berkeley National Laboratory to lead the DOE Joint BioEnergy Institute (JBEI). Each center represents a multidisciplinary partnership with expertise spanning the physical and biological sciences, including genomics, microbial and plant biology, analytical chemistry, computational biology and bioinformatics, and engineering. Institutional partners include DOE's world-class national laboratories, universities, private companies, and nonprofit organizations.

Biofuel Research Plan

In June 2006, as part of their ongoing partnership, the GTL program in DOE's Office of Biological and Environmental Research and the Office of the Biomass Program in the Department's Office of Energy Efficiency and Renewable Energy (which conducts applied research) released *Breaking the Biological Barriers to Cellulosic Ethanol: A Joint Research Agenda*. This detailed roadmap for surmounting biological challenges to cellulosic ethanol production applies to a broad array of biofuel endpoints. It provides a sound research strategy and scientific rationale for creating and operating integrated and multidisciplinary research centers, as well as opportunities for the larger research community (genomicsgtl.energy.gov/biofuels/b2bworkshop.shtml).

DOE Bioenergy Research Centers and Partners

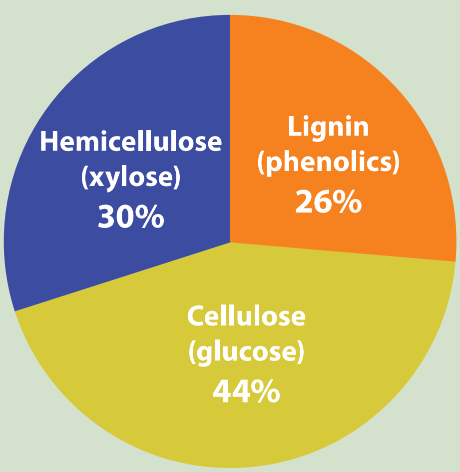


Plant Cell-Wall Recalcitrance: A Key Scientific Challenge

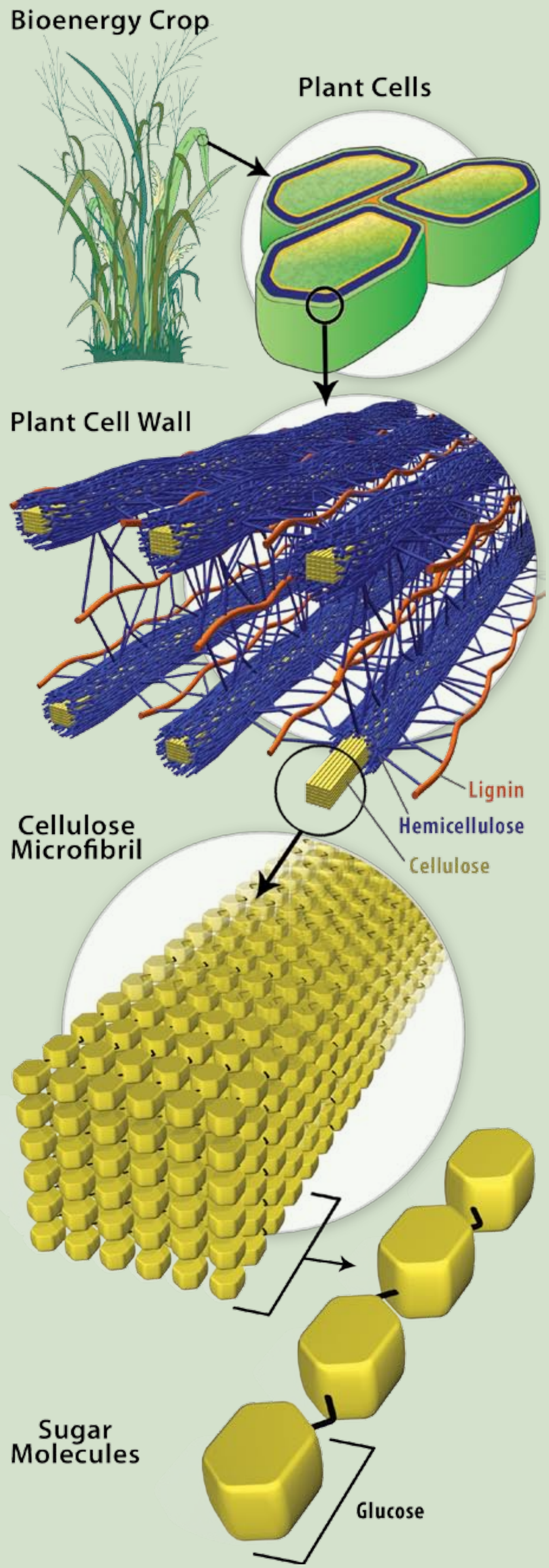
The tough structural materials in plant cell walls form a complex composite exquisitely designed to support plant structure and resist biological and chemical assaults. This natural resistance to degradation is called "recalcitrance" and represents one of the greatest challenges to attaining a cost-effective cellulosic biofuel industry.

A large portion of the plant cell wall contains long chains of sugars (polysaccharides) that can be converted to biofuels. Cellulose—the most abundant biological material on Earth—consists of tightly bound sugar chains organized into strong cable-like structures (microfibrils). Like steel girders stabilizing a skyscraper's structure, microfibrils reinforce plant cell walls. Locked away within the microfibril's sugar chains are thousands of glucose molecules, a type of six-carbon sugar readily converted into biofuels by microbes. Physically accessing these sugars, however, is difficult.

Cellulose microfibrils are embedded within a matrix of other polymers (hemicellulose and lignin). Hemicellulose, a mix of branched polysaccharides made up of five- and six-carbon sugars, links to lignin, a rigid noncarbohydrate polymer that forms a protective coating to shield cellulose and hemicellulose from enzymatic attack. In addition to serving as a physical barrier to enzymes and microbes, lignin also is a source of chemical by-products that can inhibit sugar conversion to biofuels.



Approximate abundance of the three primary components of biomass.



Biofuels: Grand Challenges for Biology

The ultimate goal for the three DOE Bioenergy Research Centers is to better understand the biological mechanisms underlying biofuel production so that those mechanisms can be redesigned, improved, and used to develop novel, efficient bioenergy strategies that can be replicated on a mass scale. Fundamental research undertaken by the centers will create the knowledge underlying three grand challenges at the frontiers of biology. The centers' research approaches and findings ultimately will benefit all biological investigations. These grand challenges include:

1. Development of next-generation bioenergy crops.
2. Discovery and design of enzymes and microbes with novel biomass-degrading capabilities.
3. Discovery and design of microbes that transform fuel production from biomass.

The science to solve these challenges remains inherently complex, requiring multiple interdisciplinary teams that approach the same problems from different directions to accelerate scientific progress (see table, DOE Bioenergy Research Center Strategies at a Glance, next page). The following sections explain some scientific issues related to these challenges.

1. Development of Next-Generation Bioenergy Crops

Bioenergy crops include grasses, trees, and other plants grown specifically for energy production. These crops and other forms of cellulosic biomass provide the raw material for bioenergy. The raw material comes from cellulose and other complex cell-wall compounds, such as lignin, that strengthen and support plant structure (see sidebar, p. 8). The primary constituents of many plant cell-wall compounds are simple sugars amenable to fermentation, producing ethanol or other biofuel chemicals. The cell walls are so complex that several thousand genes are thought to be involved in their synthesis and maintenance. Few of these genes have been identified, and little is known about their function.

By understanding the genes and mechanisms that control cell-wall synthesis in plants, scientists could develop new energy crops with altered biomass composition or modified links within and between cell-wall components. These "designer" bioenergy crops would retain robust growth in the field but could be triggered to break down rapidly in the biorefinery. Besides modification of plant cell walls, another approach to improving bioenergy crops is to increase the accumulation of starches and oils in plant tissues. Starches and oils are much easier than cellulose to convert into biofuels.

In addition to altering biomass composition, other energy-crop improvements include increasing biomass productivity per acre, increasing resistance to pests and drought, and decreasing the application of fertilizers and other inputs. Many potential energy crops are grasses or fast-growing trees that have not benefited from the years of agricultural research devoted to breeding traditional crops such as corn or wheat (see sidebar, Fundamental Research to Facilitate Bioenergy Crop Development, p. 11). Availability of more plant-genome sequence information can accelerate the development of DNA markers used to identify and isolate the many genes associated with traits that can improve energy crops. With DNA markers and other new biological tools, the time required to identify desired genetic variants and produce new energy crops ready for harvest could be reduced significantly.

2. Discovery and Design of Enzymes and Microbes with Novel Biomass-Degrading Capabilities

Nature uses both enzymes and multienzyme complexes called "cellulosomes" to break down cellulosic biomass (see sidebar, Tapping Nature's Strategies for Biomass Degradation, p. 12). The limited number of biomass-degrading enzymes and cellulosomes that have been studied perform hundreds of times more slowly than many other types of enzymes. The reasons for this are still unknown. Several factors—the nearly impenetrable architecture of plant cell walls, chemical and physical changes to biomass during pretreatment, and structural features of the enzymes—collectively contribute to the inefficient nature of biomass deconstruction. Therefore, multiple approaches must be studied simultaneously and systematically at each Bioenergy Research Center to illuminate the various processes at work.

Certain fungi and bacteria are specialists at producing enzymes that degrade biological materials in natural environments. Discovering, harnessing, and enhancing the best biomass-degrading enzymes and microbes in nature ultimately will have a significant impact on increasing the efficiency and reducing the cost of cellulosic biofuel production. Scientists are just beginning to realize the vast diversity of enzymes in environments such as the termite gut and cow rumen, and numerous natural habitats have yet to be explored. To accelerate the discovery of novel enzymes and microbes and to understand how their degradative processes work synergistically, each center is searching diverse biomass-degrading environments, from hot springs to rainforests to the guts of leaf-eating insects.

Discovering new biomass-degrading capabilities in nature is only part of the challenge. Molecular-level understanding of how enzymes and cellulosomes degrade biomass is a

DOE Bioenergy Research Center Strategies at a Glance

The complexity of the three biological grand challenges that must be overcome to achieve industrial-scale bioenergy production requires the coordinated pursuit of numerous research approaches to ensure timely success. The DOE Bioenergy Research Centers* represent a portfolio of diverse and complementary scientific strategies that will address these challenges on a scale far greater than any effort to date. Some of the strategies are listed briefly in the table below. For a more comprehensive view, see the center descriptions beginning on p. 13.

Grand Challenge: Development of Next-Generation Bioenergy Crops

Center Strategies

- **BESC** – Decrease or eliminate harsh chemical pretreatments by engineering plant cell walls in poplar and switchgrass to be less recalcitrant; simultaneously increase total biomass produced per acre.
- **GLBRC** – Engineer "model" plants and potential energy crops to produce new forms of lignin and more starches and oils, which are more easily processed into fuels.
- **JBEI** – Enhance lignin degradation in "model" plants by changing cross-links between lignin and other cell-wall components; translate genetic developments to switchgrass.

Grand Challenge: Discovery and Design of Enzymes and Microbes with Novel Biomass-Degrading Capabilities

Center Strategies

- **BESC** – Screen natural thermal springs to identify enzymes and microbes that effectively break down biomass at high temperatures; understand and engineer cellulosomes (multifunctional enzyme complexes for degrading cellulose).
- **GLBRC** – Identify combinations of enzymes and pretreatment needed to digest specific biomass types; express biomass-degrading enzymes in the stems and leaves of corn and other plants.
- **JBEI** – Improve performance and stability of enzymes harvested from the rainforest floor and other environments; engineer, through directed evolution, highly efficient cellulase enzymes.

Grand Challenge: Discovery and Design of Microbes that Transform Fuel Production from Biomass

Center Strategies

- **BESC** – Reduce the total number of cellulosic ethanol production steps by engineering a cellulose-degrading microbe to produce ethanol more efficiently.
- **GLBRC** – Reduce the total number of cellulosic ethanol production steps by engineering an efficient ethanol-producing microbe to degrade cellulose.
- **JBEI** – Connect diverse biological parts and pathways to create entirely new organisms that produce fuels other than ethanol; engineer organisms to produce and withstand high concentrations of biofuels; derive useful chemical products from lignin degradation.

***BESC: BioEnergy Science Center; GLBRC: Great Lakes Bioenergy Research Center; JBEI: Joint BioEnergy Institute**

prerequisite to designing improved processes. Because no single research approach can provide this understanding, each center is integrating different combinations of methodologies. These include high-throughput screens for proteins and metabolites, chemical analyses, state-of-the-art imaging technologies, and computational modeling to identify and characterize important factors influencing the rapid deconstruction of plant materials into sugars and other energy-rich components that can be converted to biofuels.

3. Discovery and Design of Microbes that Transform Fuel Production from Biomass

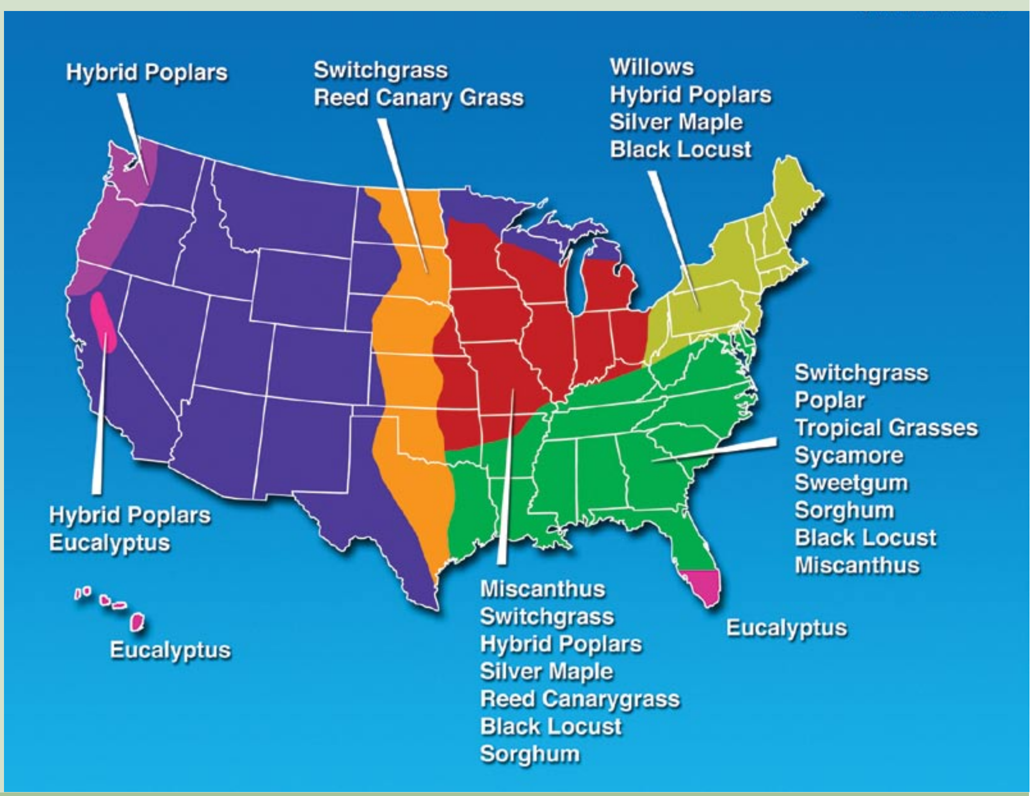
In addition to cellulose, other carbohydrates (collectively called hemicelluloses) in plant cell walls also are broken down into fermentable sugars when biomass is pretreated with heat and chemicals. Although cellulose is made of one type of six-carbon sugar (glucose) that is readily converted into ethanol and other products, microbial fermentation of the five- and six-carbon sugar mix from hemicelluloses is less efficient, thus representing a key area for improvement.

En route to the fermentation tank, biomass currently is subjected to physical, chemical, and enzymatic processing steps that can create by-products and conditions that might inhibit microbial conversion of sugars into biofuels. Ethanol and other biofuel products also inhibit microbial fermentation at high concentrations. Consequently, developing microbes robust enough to withstand the stresses of industrial processing and tolerate higher ethanol concentrations is another important research area.

Fundamental Research to Facilitate Bioenergy Crop Development

The DOE Bioenergy Research Centers are working with a few carefully selected model species of woody plants and grasses. Different genes and pathways found to improve bioenergy-related qualities in these model systems can be used to advance the development of other potential bioenergy crops that grow best in different regions of the United States (see map below).

To obtain enough biomass for large-scale production of biofuels, a variety of perennial grasses and woody crops well suited to different geographies and regional climates across the nation will need to be grown. Perennials are "low-maintenance" crops because they are not planted annually like most traditional row crops. Perennials also have longer growing seasons and require little fertilizer and other inputs. Their extensive root systems reduce erosion and increase soil quality. An additional benefit of some perennials is that a large fraction of mineral nutrients from above-ground portions of the plant are deposited underground before harvest. [Adapted from a figure produced by DOE's Oak Ridge National Laboratory Biomass Program.]



A more distant research target that could drastically simplify the entire production process is consolidated bioprocessing (CBP). This scientific strategy combines cellulose deconstruction and sugar fermentation into a single step mediated by a "multitalented" single microbe or stable mixed culture of microbes. CBP requires a redesign of microbial systems far more extensive than conventional genetic engineering approaches that involve only the modifications of a few genes associated with microbial production of a single drug or other biochemical product. A successful CBP microbe or specially designed microbial consortium may be required to produce a variety of biomass-degrading enzymes; produce minimal amounts of molecules that inhibit the overall process; ferment both five- and six-carbon sugars; and thrive in industrial reactors with high temperature, low pH, and high concentrations of biofuel products. Simultaneously incorporating so many different capabilities into a single microbe requires an unprecedented understanding of microbial systems.

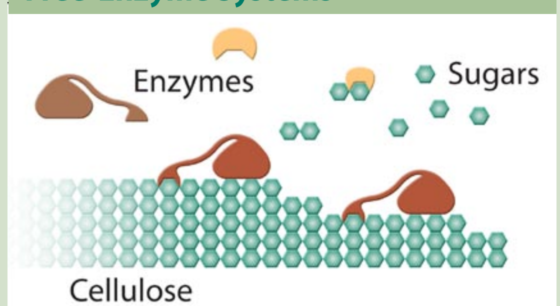
To accelerate development of the next generation of high-energy biofuels, the DOE Bioenergy Research Centers also are designing novel microbial systems that can produce biofuels other than ethanol. Some of these new fuels may be oily, petroleum-like products that are easily extracted from the watery solutions in biorefinery reactors, are compatible with existing motor vehicles and fuel transportation infrastructure, and contain as much energy per unit volume as gasoline or diesel.

Tapping Nature's Strategies for Biomass Degradation

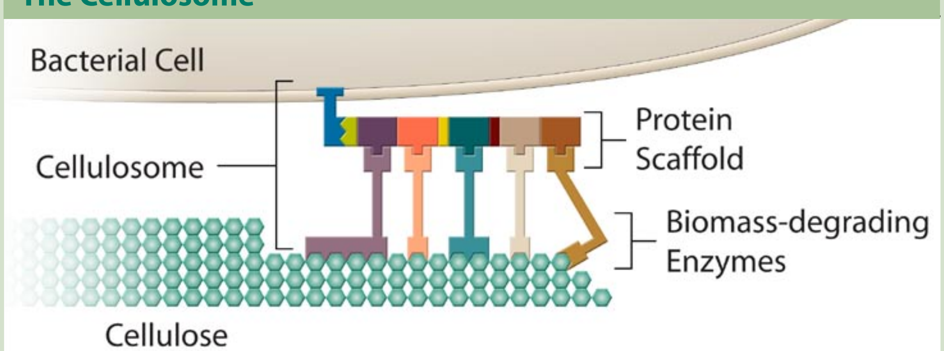
Nature has devised two types of enzyme-based strategies for breaking down plant cell walls. One strategy observed in oxygen-rich environments involves fungi and bacteria that secrete individual enzymes with complementary cell wall–degrading functions. These free enzymes work as a team to deconstruct plant cell-wall carbohydrates into simple sugars (see figure, Free-Enzyme Systems). Some of the best-studied free enzymes are cellulases secreted by *Trichoderma reesei*, a canvas-eating fungus isolated during World War II from tents and uniforms damaged by jungle rot. The DOE Bioenergy Research Centers are exploring natural environments to identify and produce new mixes of biomass-degrading enzymes that can substantially increase the efficiency of cellulosic biofuel production.

A second strategy occurring in oxygen-free environments is exhibited by bacteria that produce cellulosomes—large complexes that degrade the cell wall by assembling several different enzymes into a single protein structure. Cellulosomes protrude from bacterial surfaces, latch onto plant cell walls, and tear carbohydrates into simple sugars. *Clostridium thermocellum*, a model bacterium for studying cellulosomes, can produce more than 25 different cell wall–degrading enzymes that it can "plug and play" into its large protein scaffold (see figure, The Cellulosome). By sensing the surrounding environment, *Clostridium thermocellum* can modify the functionality of its cellulosomes on demand by assembling different combinations of enzymes to attack various compounds in the plant cell wall. The LEGO-like arrangement of enzymes in cellulosomes offers a unique opportunity to engineer "designer" multienzyme complexes targeted to specific biomass types or for different stages of biomass deconstruction.

Free-Enzyme Systems



The Cellulosome



The DOE BioEnergy Science Center (BESC), led by Oak Ridge National Laboratory (ORNL) in Oak Ridge, Tennessee, is strongly focused on the fundamental understanding and elimination of biomass recalcitrance—the resistance of cellulosic biomass to enzymatic breakdown into sugars. Recalcitrance is the single-greatest barrier to cost-effective production of biofuels. BESC's approach to making biomass easier to degrade involves (1) designing plant cell walls for rapid deconstruction and (2) engineering a multitalented microbe tailor-made for converting plants into biofuel in a single step—a strategy known as consolidated bioprocessing.

The BESC team consists of ten institutional partners and seven individual investigators with extensive experience in biomass research at other institutions (see box, BESC Partners, next page). The new Joint Institute for Biological Sciences (JIBS) systems biology research facility at ORNL serves as the central hub for coordinating research among all BESC partners.

Through understanding the root causes of biomass recalcitrance, BESC's researchers aim to reduce projected cellulosic biofuel production costs by ultimately developing new bioenergy crops and microbes that can streamline cellulosic biofuel processing. The knowledge generated by this basic research will lay the foundation for improving the productivity of various bioenergy crops, developing diverse fuel products, and ensuring sustainable cellulosic biofuel production. BESC's research is organized into three focus areas: (1) Biomass Formation and Modification, (2) Biomass Deconstruction and Conversion, and (3) Characterization and Modeling.

"By tapping nature, DOE BESC intends to replace the current expensive processes with a microbe, an enzyme, or microbe-enzyme mix that can combine multiple steps into one. For the first time, this assembles an integrated multidisciplinary team to give us the best chance to understand and overcome recalcitrance, the current bottleneck to economical, efficient bioethanol." – Martin Keller

Martin Keller
BESC Director

Martin Keller, BESC director, also leads the Oak Ridge National Laboratory Biosciences Division. Before joining ORNL, he directed technology development programs for Diversa Corporation (now Verenium), a global leader in enzyme technology, and pioneered technologies enabling single-cell microbiology.

BESC Headquarters. Oak Ridge National Laboratory's new Joint Institute for Biological Sciences facility in Oak Ridge, Tennessee, houses BESC administration and ORNL-based research staff. [Photo courtesy of Oak Ridge National Laboratory.]

Research Strategy

1. Biomass Formation and Modification

BESC biomass formation and modification research involves working directly with two potential bioenergy crops—switchgrass and poplar—to develop varieties that are easier to break down into fermentable sugars.

Currently, little is known about how cellulose and hemicelluloses are synthesized; distributed within cell walls; and attached to each other, to lignin, or to cell-wall proteins. Molecular, genetic, genomic, biochemical, chemical, and bioinformatics tools are being used to develop computational models of cell-wall biosynthesis in poplar and switchgrass. These models will help BESC researchers identify target genes and successful strategies for modifying biosynthetic pathways to generate biomass that can be readily deconstructed into sugars for biofuel production. Large numbers of plant samples will be generated and studied. By understanding how polysaccharides and lignin making up the biomass

BESC Partners

DOE's Oak Ridge National Laboratory (ORNL), Oak Ridge, Tennessee (lead institution): DOE's largest science and energy laboratory, ORNL is a world leader in poplar genome research, with strong programs in bioenergy research and plant and microbial systems biology. The ORNL Spallation Neutron Source and supercomputers at the ORNL National Leadership Computing Facility will be used to investigate and simulate the activity of enzyme complexes.

Georgia Institute of Technology, Atlanta: Georgia Tech's Institute for Paper Science and Technology provides BESC with expertise in biochemical engineering and instrumentation for high-resolution analysis of plant cell walls.

DOE's National Renewable Energy Laboratory (NREL), Golden, Colorado: NREL has nearly 30 years of experience in biomass and biofuel research and houses premiere facilities for analyzing biomass surfaces. NREL also has a long and successful history of establishing biofuel pilot plants and partnering with industry for commercial development of technologies.

University of Georgia, Athens (UGA): UGA's Complex Carbohydrate Research Center maintains state-of-the-art instrumentation for studying the structures of complex carbohydrates and the genes and pathways controlling plant cell-wall biosynthesis.

University of Tennessee, Knoxville (UT): UT conducts successful programs in bioenergy-crop genetic and field research (particularly switchgrass) and biotechnological applications of environmental microbiology.

Dartmouth College, Hanover, New Hampshire: Dartmouth's Thayer School of Engineering is a leader in the fundamental engineering of microbial cellulose utilization and consolidated bioprocessing approaches.

ArborGen, Summerville, South Carolina: ArborGen is a global leader in genetic forest research, development, and commercialization.

Verenium Corporation, Cambridge, Massachusetts: Verenium is a biofuels-focused biotechnology company and developer of high-performance specialty enzymes found in diverse natural environments and optimized for targeted applications.

Mascoma Corporation, Boston, Massachusetts: Mascoma is a leader in developing advanced bioprocessing technologies and establishing cellulosic ethanol production facilities.

The Samuel Roberts Noble Foundation, Ardmore, Oklahoma: This nonprofit organization is devoted to improving agricultural production and advancing the development of switchgrass and other grasses through genomic research.

Individual researchers from the University of California, Riverside; DOE Brookhaven National Laboratory (Upton, New York); Cornell University (Ithaca, New York); Virginia Polytechnic Institute and State University (Blacksburg, Virginia); University of Minnesota (St. Paul, Minnesota); and Washington State University (Pullman, Washington) specialize in biomass pretreatment, characterization of plant-associated microbes, cellulose and enzyme modeling, consolidated bioprocessing, and lignin biochemistry.

are synthesized and assembled, BESC researchers will develop methods for reducing cell-wall recalcitrance that can be applied to a wide range of woody and herbaceous plants.

2. Biomass Deconstruction and Conversion

Two key hypotheses drive BESC's biomass deconstruction and conversion research: (1) microorganisms can be engineered to enable consolidated bioprocessing (CBP), a game-changing, one-step, microbe-mediated strategy for directly converting plant biomass into ethanol; and (2) enzymes and microbial biocatalysts can be engineered to synergize with recalcitrance-reducing plant modifications to achieve better biomass deconstruction.

A model organism for CBP development is *Clostridium thermocellum*, a bacterium that rapidly degrades pure cellulose and then ferments the resulting sugars into ethanol (see image, BESC Bioenergy Research, next page). This microbe's strategy for combined biomass deconstruction and conversion employs cellulosomes—multifunctional enzyme complexes that specialize in degrading cellulose. Cellulosomes must be understood for rapid improvement in the deconstruction of more complex plant cell walls. BESC is studying the structures and activities of these multienzyme complexes to design new variants with better cell wall–deconstruction capabilities. In addition to working with *C. thermocellum*, BESC researchers are investigating samples from hot springs at Yellowstone National Park to identify heat-tolerant enzymes and microbes with superior biomass-degrading functions that can be used to discover additional strategies for new CBP microorganisms.

BESC will explore several fundamental frontiers: (1) mining the natural diversity of biomass-degrading enzymes and microbes, (2) studying how different biomass features affect the activities of enzymes and microbes, (3) examining the relationship between enzyme structure and function, (4) investigating how enzymes and microbes interact with pretreated cell walls, and (5) testing strategies for using pure or mixed microbial cultures for biomass deconstruction and conversion. An overarching goal is to integrate information obtained from these various investigations into comprehensive conceptual and computational models of cellulose deconstruction in both natural and engineered environments.

BESC Bioenergy Research. Babu Raman works in the Bioconversion Laboratory at Oak Ridge National Laboratory with samples of *Clostridium thermocellum*, a microbe that could simplify future cellulosic biofuel production. [Photo courtesy of Oak Ridge National Laboratory.]

3. Characterization and Modeling

Characterization and modeling researchers apply and create advanced technologies to analyze chemical and structural changes that occur in modified plant cell walls. Switchgrass and poplar samples generated by BESC researchers will be catalogued, bar coded, and analyzed in detail for chemical composition at the National Renewable Energy Laboratory (NREL). From NREL, samples are passed along to other partner institutions for pretreatment and enzyme-digestibility studies.

Knowledge gained by thoroughly characterizing and modeling cell-wall synthesis pathways, biomass structure and composition, and microbe-enzyme interactions with biomass surfaces will drive the coordinated development of CBP microbes and new generations of switchgrass and poplar optimized for deconstruction. Combining characterization, modeling, and data sharing will help define the genomic and physical basis of plant cell-wall recalcitrance and deconstruction.

Translation of BESC Science into Commercial Applications

BESC has recruited internationally known academic and bioenergy industry leaders to serve on its board of directors. BESC also has formed a commercialization council of technology-transfer experts from the center's partner institutions to evaluate the commercial potential of all new inventions arising from BESC research. BESC will host a BioEnergy Nexus forum that will bring together graduate students with innovative product ideas, bioenergy companies, venture capitalists, and other investors to catalyze new collaborations.

BESC's home base will be less than 40 miles from the nation's largest precommercial switchgrass-to-ethanol demonstration plant. The $40 million facility is funded by the Tennessee Biofuels Initiative and will be operational in 2009. The demonstration plant will be a useful resource for testing the commercial viability of switchgrass varieties and biofuel-processing technologies developed from the scientific discoveries of BESC and other research organizations.

Education and Outreach

By leveraging successful educational and training programs already in place at partner academic institutions, BESC will offer students, postdoctoral staff, and scientists interdisciplinary research opportunities that cut across a broad range of biofuel-related fields. To extend the reach of BESC science to diverse locations and communities, collaborative workshops for training students and scientists and an open seminar series reporting scientific progress will be held at each partner institution. BESC also will provide opportunities each year for non-BESC scientists to participate in research at one or more partner sites. Announcements about BESC outreach and educational programs and employment opportunities will be posted on the BESC website (bioenergycenter.org).

DOE Great Lakes Bioenergy Research Center

greatlakesbioenergy.org

The DOE Great Lakes Bioenergy Research Center (GLBRC) is led by the University of Wisconsin–Madison, in close partnership with Michigan State University (see box, GLBRC Partners, next page). Located in the world's most productive agricultural region, the GLBRC is exploring scientifically diverse approaches to converting sunlight and various plant feedstocks—agricultural residues, wood chips, and grasses—into biofuels. In addition to its broad range of scientific research projects, the GLBRC is collaborating with agricultural researchers and producers to help develop the most economically viable and environmentally sustainable practices for bioenergy production. The new GLBRC facility is part of the University of Wisconsin–Madison campus.

GLBRC scientific research is organized into five focus areas:

1. Improving Plant Biomass
2. Improving Biomass Processing
3. Improving Biomass Conversion
4. Fostering Sustainable Bioenergy Practices
5. Creating Technologies to Enable More Advanced Bioenergy Research

"The scientists of the DOE Great Lakes Bioenergy Research Center are eager to help solve what is arguably the largest socially, environmentally, politically, and economically significant challenge of our time—the need for new, renewable sources of energy."
– Tim Donohue

Tim Donohue
GLBRC Director

Tim Donohue is the GLBRC principal investigator and director, as well as a Professor of Bacteriology at the University of Wisconsin–Madison. He is an expert in applying the latest genomic and systems biology approaches to understanding how genetic pathways and networks in microorganisms are used to generate cell biomass or biofuels from sunlight.

GLBRC Facility. University of Wisconsin–Madison's new Microbial Sciences Building houses GLBRC administration and scientific research. [Photo by Wolfgang Hoffmann, University of Wisconsin–Madison.]

Research Strategy

1. Improving Plant Biomass

In addition to investigating how genes affect cell-wall digestibility in model plants, cornstalks, and switchgrass, GLBRC researchers will be breeding plants that produce more hemicelluloses, starches, oils, or new forms of lignin that are easier to process into fuels. Plant oils have twice the energy content of carbohydrates and require little energy to extract and convert into biodiesel. Soybean oil is used primarily to produce biodiesel in the United States; however, oil yield per acre of soybeans needs to be improved. GLBRC researchers aim to increase the energy density of grasses and other nontraditional oil crops by understanding and manipulating the metabolic and genetic circuits that control accumulation of oils and other easily digestible, energy-rich compounds in plant tissues.

2. Improving Biomass Processing

Located at the intersection of America's agricultural heartland and its abundant northern forest biomass, the GLBRC has access to a rich diversity of raw biomass for study.

GLBRC biomass-processing research will discover and improve natural cellulose-degrading enzymes extracted from diverse environments (see image, The Search for Cellulose-Degrading Enzymes, next page). Improved enzymes created by the GLBRC protein-production pipeline are used in analyzing a range of plant materials and pretreatment conditions to identify the best combination of enzymes, chemicals, and physical processing for enhancing the digestibility of specific biomass sources. GLBRC researchers will identify and quantify small molecules generated by different pretreatment methods and examine how these molecules impact biofuel yield.

To decrease the costs of producing and using enzymes to break down cellulose in plants, researchers in this focus area are working with plant-biomass researchers. They are expressing biomass-degrading enzymes in the stems and leaves of corn and other plants—essentially designing plants to "self-destruct" on cue in the biofuel-production facility.

3. Improving Biomass Conversion

GLBRC biomass-conversion research is driven by the need to increase the quantity, diversity, and efficiency of energy products derived from plant biomass. Cellulosic ethanol is a major focus for GLBRC research, but the center also aims to improve both biological and chemical methods for converting plant material into hydrogen, electricity, or other chemicals that can replace fossil fuels (see image, Biodiesel Production Research, next page). In addition to converting plants into energy, GLBRC researchers are developing microbes that directly convert sunlight into hydrogen or electricity.

To create a microbe capable of carrying out all biologically mediated biofuel-production steps, GLBRC scientists are taking a somewhat novel approach. Instead of modifying an effective biomass-degrading microbe to produce ethanol, the researchers are starting with efficient ethanol-producing microbes and engineering them to produce enzymes and pathways to break down cellulose.

4. Fostering Sustainable Bioenergy Practices

For the bioenergy economy to have a positive impact on the United States, complex issues in agricultural, industrial, and behavioral systems must be addressed. To create a better understanding of the larger context that ultimately influences the direction and acceptance of new biotechnologies, GLBRC

GLBRC Partners

University of Wisconsin–Madison (lead institution): The GLBRC's lead partner provides world-renowned expertise in genome-enabled analysis of plant and microbial pathways, networks, and systems; computational analysis of bioenergy proteins, organisms, and ecosystems; and discovery, production, and improvement of bioenergy enzymes.

Michigan State University (MSU), East Lansing: MSU researchers are experts in the breakdown and synthesis of plant cell walls, oils, and other polymers; the breakdown of cellulose in plant stems, stalks, and leaves, including trees and other woody plants; and the development of biofuel-production practices that are both environmentally and economically sustainable.

University of Florida, Gainesville: This GLBRC partner institution brings expertise in the conversion of lignocellulosic biomass into ethanol using novel bacterial agents.

Iowa State University (ISU), Ames: ISU researchers are experts in constructing economic models of biomass practices.

Illinois State University, Normal: Researchers at Illinois State University work on the genetic and molecular analysis of switchgrass.

Lucigen Corporation, Middleton, Wisconsin: Lucigen provides valuable expertise in bioprospecting for new biomass deconstruction enzymes.

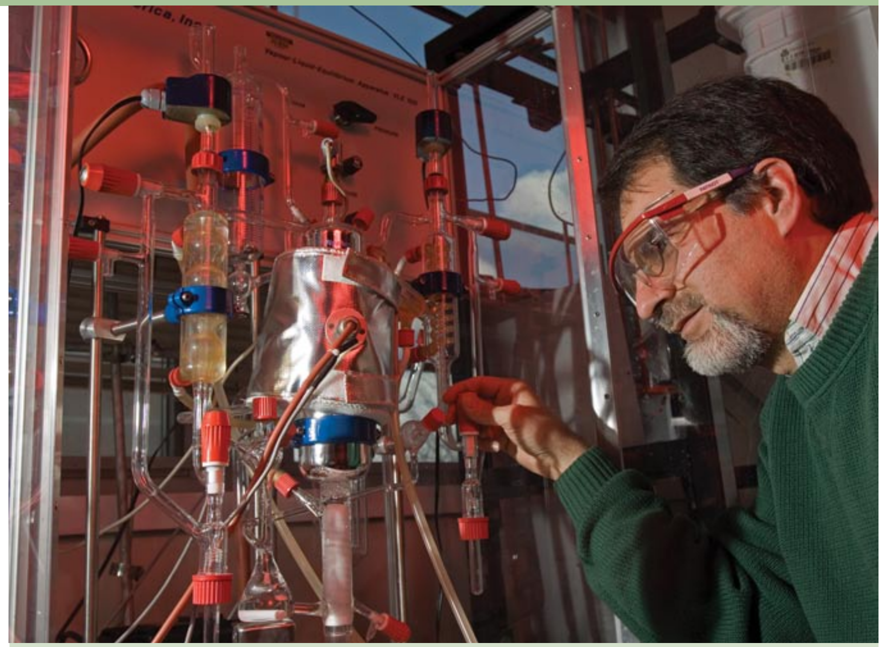
DOE's Oak Ridge National Laboratory (ORNL), Oak Ridge, Tennessee: ORNL will enable the GLBRC to evaluate biomass sustainability by modeling ecosystem changes that could result from the biofuel production cycle.

DOE's Pacific Northwest National Laboratory (PNNL), Richland, Washington: PNNL enables the GLBRC to complete high-throughput analysis of bioenergy proteins and organisms and analyze the entire life cycle of bioenergy practices.

The Search for Cellulose-Degrading Enzymes. To discover and improve enzymes for biomass deconstruction, GLBRC researchers are conducting high-throughput screens of genetic material from specialized ecosystems such as bacteria that live in association with tropical leaf-cutting ants. [Photo by Wolfgang Hoffmann, University of Wisconsin–Madison.]

scientists plan to examine the environmental and socioeconomic dimensions of converting biomass to biofuel.

To determine the best practices for biofuel production, GLBRC researchers will study issues such as minimizing energy and chemical inputs for bioenergy-crop production; reducing greenhouse gas emissions from the entire biofuel-production life cycle; and understanding the environmental impacts of removing leftover stalks, stems, and leaves from food crops. GLBRC scientists also will study the social and financial incentives needed to promote the adoption of more environmentally beneficial practices.



Biodiesel Production Research. Michigan State University scientist and GLBRC researcher Carl Lira works with a conceptual setup for the biodiesel continuous production process. This process may eliminate harmful by-products of biodiesel production and generate substances that could be used in either fuel or consumer products. [Photo by Kurt Stepnitz, Michigan State University.]

5. Creating Technologies to Enable More Advanced Bioenergy Research

This focus crosses all areas of research by providing cutting-edge, genome-based technologies that enable the innovative discoveries and creative solutions needed to advance bioenergy research. GLBRC researchers will deploy high-throughput, automated screens for genes and proteins in plants and microbes that affect biomass and biofuel production; integrate information from multiple research approaches; and develop predictive models for relevant enzymes, pathways, or networks that can guide the development of new plants, enzymes, or microbes that would be useful in a biofuel-production pipeline.

Industry Partnerships

The GLBRC will generate linkages with the private sector that will help bring technologies to the marketplace. New technologies developed at the GLBRC will be tested in production-line facilities.

Education and Outreach

With a history of excellence in the land-grant missions of education, training, and outreach, GLBRC academic partners are deeply committed to training the bioenergy leaders of tomorrow, while removing today's bottlenecks in the biofuel pipeline. The partners will offer new bioenergy-focused summer research programs, labs, seminars, and special courses. By working with existing programs at university partners, GLBRC scientists also plan to develop workshops and educational modules for K–12 teachers on carbon chemistry, sustainability, and biodiversity issues related to biofuel production. Additionally, GLBRC researchers will develop informative materials and host public forums to raise awareness of and generate support for biofuels among farmers and communities.

DOE Joint BioEnergy Institute

jbei.org

Research at the DOE Joint BioEnergy Institute (JBEI) is using the tools of synthetic biology to produce the next generation of biofuels. JBEI is engineering microbes and enzymes to process the complex sugars of cellulosic biomass into biofuels that can directly replace gasoline. By developing new bioenergy crops, JBEI will transform lignin into a source of valuable new products. A six-institution partnership led by Lawrence Berkeley National Laboratory, JBEI is based in the San Francisco Bay Area (see box, JBEI Partners, next page), which is fast becoming a hub of renewable energy research and development. JBEI is headquartered in a new laboratory in Emeryville, California, centrally situated among the partner institutions.

JBEI's research strategy revolves around four interdependent efforts that focus on (1) developing new bioenergy crops, (2) enhancing biomass deconstruction, (3) producing new biofuels through synthetic biology, and (4) creating technologies that advance biofuel research.

Research Strategy

1. Developing New Bioenergy Crops

To increase our understanding of genes and enzymes involved in the synthesis and modification of plant cell walls, JBEI researchers are using well-characterized genomes and genetic-engineering tools established for rice and *Arabidopsis* (a small flowering plant related to mustard). These two model systems are ideal research subjects because they go from seed to mature plant in weeks or months, rather than the year or more required for energy crops such as switchgrass and poplar. Genetic insights from rice (a model for grasses) and *Arabidopsis* (a model for trees) will accelerate the development of new energy crops.

In addition, JBEI researchers are investigating metabolic pathways involved in lignin biosynthesis. The research may lead to development of plants that can be deconstructed more easily. This unique basic research program could help to transform lignin into a valuable source of chemicals and polymers, while also improving the economics of converting cellulosic biomass into fuels.

JBEI

JOINT BIOENERGY INSTITUTE

"DOE JBEI is designed to be an engine of ingenuity, dynamically organized with all the scientific teams working together in a single location to enable researchers to share ideas and address cellulosic biomass problems at a systems level. Within 60 miles of JBEI, we have available some of the world's foremost authorities on energy, plant biology, systems and synthetic biology, imaging, nanoscience, and computation, plus the highest concentration of national laboratories and research universities in the nation." – Jay Keasling

Jay Keasling
JBEI Chief Executive

Jay Keasling is the JBEI Chief Executive, director of Berkeley Lab's Physical Biosciences Division, and a U.C. Berkeley Professor of Chemical Engineering. He also is an award-winning scientific researcher and leading authority in the burgeoning field of synthetic biology.

JBEI Research Facility. JBEI researchers are located at a single site in Emeryville, California. [Photo by Roy Kaltschmidt, Berkeley Lab.]

2. Enhancing Biomass Deconstruction

JBEI researchers are developing new pretreatments and enzymes that enhance cellulose conversion to sugars and minimize toxic by-products (see image, Pretreatment Research at JBEI, below). As part of this effort, they are exploring a broad range of biomass environments, from rainforests to compost, to discover and isolate new enzymes that more efficiently degrade cellulose and lignin. Their studies of the mechanisms of biomass deconstruction at the molecular level will enable new insights and approaches for the efficient conversion of all plant components to useful products.

3. Producing New Biofuels Through Synthetic Biology

JBEI researchers are applying synthetic biology approaches to engineer microorganisms that convert the sugars released from biomass deconstruction into ethanol and other, more advanced biofuels such as longer alcohols and alkanes. These next-generation biofuels will yield almost as much

JBEI Partners

DOE's Lawrence Berkeley National Laboratory (LBNL), Berkeley, California (lead institution): LBNL, a multidisciplinary national laboratory, is home to the Advanced Light Source, the Molecular Foundry, the National Center for Electron Microscopy, and the National Energy Research Scientific Computing Center. LBNL also is a founding partner of the DOE Joint Genome Institute, one of the world's largest and most productive DNA sequencing centers.

DOE's Sandia National Laboratories (SNL), Albuquerque, New Mexico, and Livermore, California: SNL is a multidisciplinary national laboratory that hosts DOE's Combustion Research Facility, a premier center for combustion science, and is a partner in DOE's Sun Lab, a virtual laboratory for the study of solar-power technologies.

DOE's Lawrence Livermore National Laboratory (LLNL), Livermore, California: LLNL, a multidisciplinary national laboratory, is home to the Center for Accelerator Mass Spectrometry and the world's fastest supercomputer, the BlueGene/L. LLNL also is one of the DOE Joint Genome Institute's founding partners.

University of California, Berkeley: This university is ranked first by the National Research Council for distinguished scholarship and is home to the Synthetic Biology Engineering Research Center and the Energy Biosciences Institute.

University of California, Davis: U.C. Davis oversees the California Biomass Collaborative and is home to the Northern California Nanotechnology Center, the Western Regional Center of the National Institute for Global Environmental Change, and the U.C. Davis Genome Center.

Carnegie Institution (CI) Department of Plant Biology, Palo Alto, California: CI is a private, nonprofit organization. Its Department of Plant Biology at Stanford University maintains TAIR, a comprehensive database on *Arabidopsis thaliana*, the model organism for plant molecular genetics.

Pretreatment Research at JBEI. JBEI researchers Seema Singh (shown here) and Blake Simmons study pretreatments that could facilitate the conversion of switchgrass biomass into liquid fuels. [Photo by Randy Wong, Sandia National Laboratories.]

energy per volume as gasoline and will be transportable through existing fuel pipelines (see sidebar, Synthetic Biology, this page). Biologically produced alkanes and other oil-like hydrocarbons could replace gasoline in today's cars on a gallon-for-gallon basis.

Mathematical models of metabolism and gene regulation, developed from detailed understanding of *Escherichia coli* and *Saccharomyces cerevisiae* (yeast) biology, will guide the design and construction of new microbes for biofuel synthesis.

4. Creating Technologies that Advance Biofuel Research

JBEI researchers are creating new, broadly applicable technologies to advance research that will speed the development of biofuels. Among these technologies is a novel chip-based system that can be used to identify new enzymes with cellulose- and lignin-degrading activities. In addition, JBEI researchers are constructing automated microfluidic platforms that can simultaneously screen hundreds of enzymatic reactions to help identify the best enzymes for biomass deconstruction. Technologies also are being developed for rapid high-resolution imaging to visualize and characterize the effects of pretreatment protocols on plant biomass. These and other enabling technologies are expected to generate large volumes of data that will be collected and catalogued in a centralized database, then analyzed using new bioinformatics tools.

Industry Partnerships

To promote the transfer of JBEI inventions to private industry for commercial development that can benefit the nation, JBEI is establishing collaborations with companies that have relevant scientific and marketing capabilities in energy, agribusiness, and biotechnology. The JBEI Industry Partnership Program provides companies with opportunities to contribute to JBEI and become part of the JBEI community. To further help ensure that its science will ultimately be able to serve national needs, JBEI has established an advisory committee with representation from the entire spectrum of the biofuel industry.

Education and Outreach

Educational efforts at JBEI build on strong undergraduate, graduate, and postdoctoral training programs, established technical training and seminar programs, and nationally recognized K–12 and community-college science outreach programs already in place at JBEI's member institutions. In addition to starting a new student fellowship program, JBEI will collaborate with U.C. Berkeley's Management of Technology Program to enable young scientists and engineers to develop biofuel-related business plans.

Synthetic Biology

Building Novel Biological Systems for Useful Purposes

Synthetic biologists design and build novel organisms to generate products not made by natural systems. This process may involve constructing entirely new biological systems from a set of standard parts—genes, proteins, and metabolic pathways—or redesigning existing biological systems. The tools of synthetic biology also can be used to study the interior of living cells at the molecular level, providing critical new information and insight into the machinery of life and the natural world. Synthetic biology holds promise for advances in many areas, including the development of renewable, carbon-neutral energy sources, nonpolluting biological routes for the production of chemicals, safer and more effective pharmaceuticals, and better environmental remediation technologies.

At JBEI, researchers will use synthetic biology to develop new platform hosts for producing enzymes and fuels and to create biomolecular parts and devices for constructing new fuel-generating organisms and improved plants. Among other advances, such goals will be achieved through the improved capabilities of fermentative organisms to tolerate processing conditions and inhibit unwanted by-products. Capabilities also will be engineered into fuel-producing organisms to convert five-carbon sugars into fuel and make use of lignin monomers. Following the strategy that biological systems can be revamped more effectively or built from scratch if standardized parts are employed, investigators will assemble a catalog of well-characterized biosynthetic components to help in designing, testing, optimizing, and implementing integrated large-scale biosynthetic units. These tools and principles, used by JBEI Chief Executive Jay Keasling to develop a relatively inexpensive synthetic biology alternative for producing the antimalarial drug artemisinin, will aid in developing the next generation of biofuels.

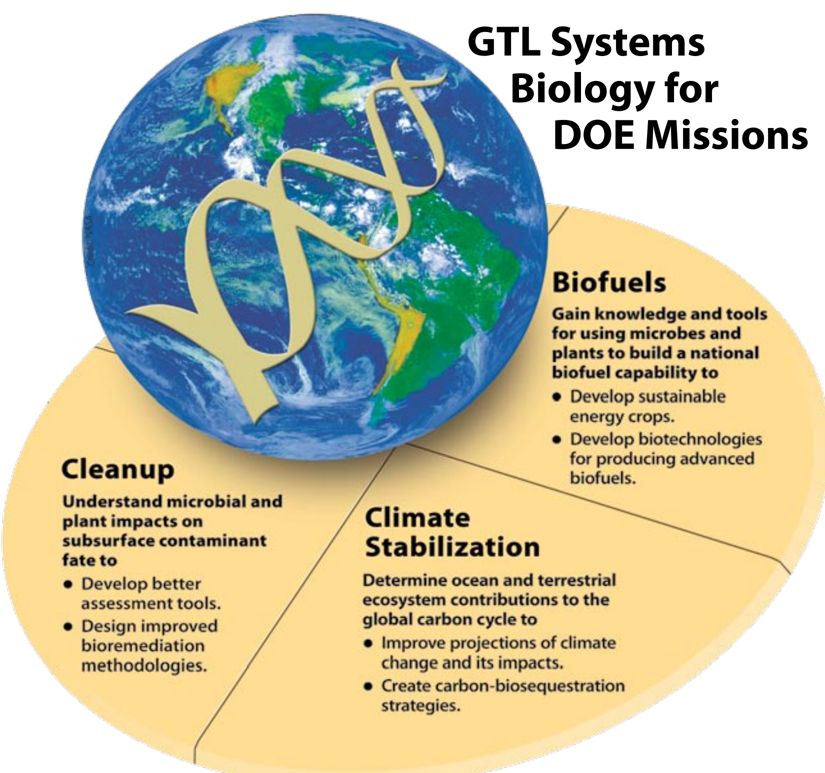
Genomics:GTL Program
From Genome Sequences to Systems Understanding

genomicsgtl.energy.gov

Genomics:GTL (GTL, formerly Genomes to Life) is a research program that aims to develop a predictive understanding of biological systems relevant to energy production and other Department of Energy (DOE) missions in environmental remediation and climate change mitigation (see illustration, GTL Systems Biology for DOE Missions, this page).

GTL research is conducted at national laboratories and universities and includes single-investigator projects, multi-institutional collaborations, and fundamental research centers. GTL is run by the Office of Biological and Environmental Research (OBER) in partnership with the Office of Advanced Scientific Computing Research, both within DOE's Office of Science.

The DNA sequence of an organism's complete genome is the starting point to understanding any biological system. Scientists from the three Bioenergy Research Centers and other GTL projects are working with the DOE Joint Genome Institute to sequence the genomes of energy-related plants, as well as microbes and fungi that degrade biomass or impact plant productivity. Building on this foundation of genomic information, the whole-systems understanding of biology generated by GTL will enable scientists to redesign proteins, biochemical pathways, and even entire plants or microbes important to solving bioenergy challenges and meeting other DOE needs. Even though the specific functions of these systems vary, common fundamental principles control the behavior of all biological systems. Knowledge of these underlying principles will advance biological solutions to DOE missions.



Several developments have converged in recent years to suggest that GTL systems biology research into microbes and plants may be able to overcome critical roadblocks to large-scale production of fuels from plant biomass. The ability to rapidly sequence the DNA of any organism is a critical but modest part of these new capabilities. Others include:

- Development of high-throughput techniques and commercially available reagents for protein production and characterization to test thousands of natural and engineered protein variations.
- Emergence of a range of new instrumentation for observing proteins and other cell constituents to determine, for example, how cell walls are constructed.
- Availability of technologies for high-resolution imaging from molecular to cellular to microbial-community spatial scales that can be used to help understand, for example, why rates of cellulose degradation vary.
- Major advances in computational capability.

In addition to GTL, OBER is supporting related genomic bioenergy collaborative research with other government agencies. A research program jointly sponsored by OBER and the U.S. Department of Agriculture (USDA) Cooperative State Research, Education, and Extension Service's National Research Initiative supports genome-based approaches to accelerate plant-breeding programs and improve potential bioenergy crops. DOE and USDA also are working together to identify and understand sustainability issues associated with a rapid scaleup of biofuel production.

DOE Office of Science

The Department of Energy's (DOE) Office of Science is the nation's single-largest supporter of basic research in the physical sciences and helps ensure U.S. world leadership across a broad range of scientific disciplines. The Office of Science supports a diverse portfolio of research at more than 300 colleges and universities nationwide and manages 10 world-class national laboratories with unmatched capabilities for solving complex interdisciplinary scientific problems. It also builds and operates the world's finest suite of scientific facilities and instruments used by more than 21,000 researchers in Fiscal Year 2007 to extend all areas of science.

For More Information

DOE Bioenergy Research Centers
genomicsgtl.energy.gov/centers/

BioEnergy Science Center (BESC)
bioenergycenter.org

Great Lakes Bioenergy Research Center (GLBRC)
greatlakesbioenergy.org

Joint BioEnergy Institute (JBEI)
jbei.org

Genomics:GTL
genomicsgtl.energy.gov

DOE Mission Focus: Biofuels
genomicsgtl.energy.gov/biofuels/

DOE–USDA Plant Feedstock Genomics for Bioenergy
genomicsgtl.energy.gov/research/DOEUSDA/

DOE Joint Genome Institute
jgi.doe.gov

Breaking the Biological Barriers to Cellulosic Ethanol: A Joint Research Agenda
genomicsgtl.energy.gov/biofuels/b2bworkshop.shtml

Twenty in Ten Initiative from the President's 2007 State of the Union Address
whitehouse.gov/stateoftheunion/2007/initiatives/energy.html

DOE Office of Biological and Environmental Research
science.doe.gov/ober/

DOE Office of Science
science.doe.gov

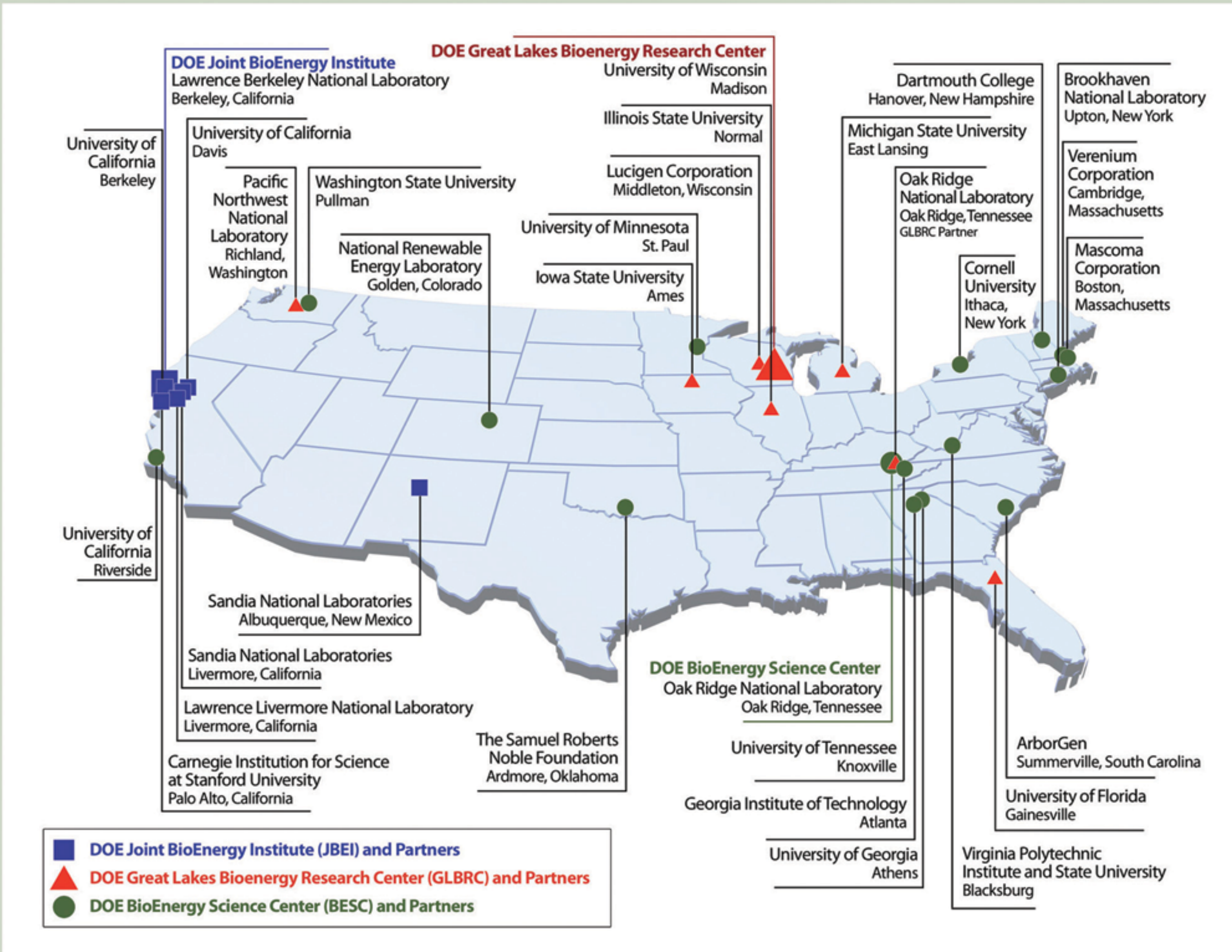
DOE Office of Biological and Environmental Research

The Office of Science's Office of Biological and Environmental Research (OBER) is the home of the Genomics:GTL program. OBER supports DOE's mission of world-class fundamental scientific research through peer-reviewed multidisciplinary projects in the following areas.

- **Life Sciences:** Provide the fundamental scientific understanding of plants and microbes necessary to develop new robust and transformational basic research strategies for producing biofuels, cleaning up waste, and sequestering carbon.
- **Climate Change Research:** Deliver improved scientific data and models on the potential response of the Earth's climate and terrestrial biosphere to increased greenhouse gas levels so policymakers can determine safe levels of greenhouse gases in the atmosphere.
- **Environmental Remediation:** Provide sufficient scientific understanding to allow DOE sites to incorporate coupled physical, chemical, and biological processes into decision making for environmental remediation and long-term stewardship.
- **Medical Applications and Measurement Science:** Develop intelligent biomimetic electronics that can both sense and correctly stimulate the nervous system.
- **Facilities:** Manage facility operations to the highest standards of overall performance using merit evaluations with independent peer review.

In the grand tradition of DOE's basic research initiatives, the Bioenergy Research Centers grew from DOE's historic role in sequencing the human genome. The Department initiated the Human Genome Project; founded the DOE Joint Genome Institute, one of the world's largest and most productive public genome sequencing centers; and completed the sequencing of three human genome chromosomes.

TRANSFORMATIONAL BIOLOGY FOR ENERGY BREAKTHROUGHS



DOE Bioenergy Research Centers and Partners

http://genomicsgtl.energy.gov/centers/

DOE BioEnergy Science Center (BESC)

bioenergycenter.org

DOE Great Lakes Bioenergy Research Center (GLBRC)

greatlakesbioenergy.org

DOE Joint BioEnergy Institute (JBEI)

jbei.org

U.S. Department of Energy February 2008