The mission of the National Agricultural Genotyping Center is to translate scientific discoveries into solutions for production agriculture, food safety, functional foods, bioenergy and national security.
The mission of the National Agricultural Genotyping Center (NAGC) is to translate scientific discoveries into solutions for production agriculture, food safety, functional foods, bioenergy and national security.

I. The Situation at Hand

“... the safest bet in America is American agriculture.”
Thomas Vilsack, Secretary of Agriculture, U.S. Department of Agriculture

The abundance of American agriculture is astonishing. Armed with technologies and practices unknown to the previous generation, today’s farmers produce yields on the same acreage that their parents never thought possible. However, if U.S. agriculture is going to continue this trend amid the pressures of market volatility and a growing world population, this country must pursue investments in research and technology infrastructure that demonstrate the quickest and greatest returns.

In analyzing the current state of research and technology in the U.S. agricultural sector, the greatest opportunity to capture returns resides in the efficient utilization of critical processes, highly-specialized expertise and breakthrough technologies. Specifically, this entails the application of genomic information through genotyping to develop new traits and products for the purpose of improving production agriculture’s performance and protecting our food supply.

At present, there exists a large unmet need for high-throughput genotyping services within U.S. agricultural research. The National Corn Growers Association in partnership with Los Alamos National Laboratory and the Donald Danforth Plant Science Center proposes the establishment of a national center for agricultural genotyping to address this need by alleviating the inefficiencies, redundancies, bottlenecks and gaps that impede commercial development. The proposed National Agricultural Genotyping Center (NAGC) will contribute to maintaining the safety of our food supply, economic stability and national security by making high-throughput genotyping available to both private and public scientists from breeders all the way to quality control and food safety scientists.
II. Maintaining Global Leadership

“Our continued global leadership and success depends upon a renewed and reinforced commitment to our world-class agricultural science and research capabilities.”
Catherine Woteki, USDA Under Secretary for Research, Education & Economics.

<table>
<thead>
<tr>
<th>Period</th>
<th>Growth</th>
</tr>
</thead>
<tbody>
<tr>
<td>1960-1979</td>
<td>Grew 3.2%</td>
</tr>
<tr>
<td>1980-1989</td>
<td>Flat</td>
</tr>
<tr>
<td>1990-1999</td>
<td>Grew 0.6%</td>
</tr>
<tr>
<td>2000-2009</td>
<td>Decreased 0.2%</td>
</tr>
</tbody>
</table>

Federal Agricultural Research Expenditures

According to the USDA NAREEE report (2011), with a lag time of 25 years from research to commercialization, the U.S. is now paying for our lack of investment in agricultural research. Their conclusions were:

- by 2050, the worldwide demand for food and fiber is expected to grow by 70 percent.
- that funding for production agricultural research must be dramatically increased to keep American farmers competitive in future international markets.
- that the US is paying for decades of flat or decreased funding for production agricultural research. US agriculture is a net exporter of products and this is very important for the economy therefore funding for agricultural research must be dramatically increased to keep the US an exporter of food and fiber.
- that worldwide demand for food, fiber and fuel cannot be met without a strong, well funded US production agricultural initiative.
- historically, high return on public agricultural research funding is due to its focus on improving production practices, genetic improvement and new uses. Unfortunately these areas of research are receiving less funding.
- that the composition of agricultural funding has moved away from production agriculture.
- data from developing countries shows China, India and Brazil are the largest public investors in production agricultural research and these countries will be the largest competitors to US agricultural products in the future.

Historically, American agriculture has experienced incredibly high levels of productivity. For example, in 1960 one acre of land could yield 55 bushels of corn. Today, one acre can yield over 157 bushels. U.S agriculture returns $10 to the economy for every research dollar spent. Because returns are so high, investment in agricultural research and technology is the most effective means for generating economic welfare.

Agriculture has always been critical to the economic prosperity of our nation. Today, the U.S. agriculture and food industry adds $1 trillion to our economy and accounts for 13 percent of U.S.
gross national product. However, the industry is not without challenges. In addition to constant and aggressive competition from foreign producers, our national food supply is regularly under the threat of natural pathogens. Centralizing our nation’s agricultural genotyping work will provide the necessary low cost and high-throughput genetic tests necessary to accelerate U.S. breeding, production research and ensure consumer safety.

Investments in such a center will directly translate into economic gains. As proposed, the NAGC would provide the necessary technology to ensure food safety, increase agricultural production, proactively monitor livestock and agricultural goods for diseases and advance breeding.

The most efficient method to address the detection and monitoring of pathogens and the identification of genetic traits is through genotyping. However, currently the genotyping services needed to adequately ensure consumer safety, protect producers and increase production levels are fragmented, inefficient and inadequate. The result is significant and unnecessary waste of financial, human and computing resources, failure to quickly respond to agricultural challenges, lost market opportunities and an inability to adequately safeguard U.S. citizens. By providing an economical, high-throughput, and broadly applicable genotyping service, the NAGC will meet the sector-wide need for agriculture genotyping.

III. Improving the Agricultural Sector

“There is no other arena of economic activity, or field of science and innovation, that so directly addresses human survival and quality of life, global economic development, and prospects for an environmentally sustainable future as agriculture and agbioscience.”


Food safety and security

“There are certain things only a government can do. And one of those things is ensuring that the foods we eat are safe and do not cause us harm,”

President Barack Obama

The NAGC's ability to rapidly test samples of agricultural products for the presence of pathogens prior to wide-scale distribution will improve consumer confidence in the food supply and mitigate the economic impact of contamination events. History has shown that failure to detect product contamination early can lead to the mixing of compromised and uncompromised goods, exacerbating the scale and scope of product recalls. These recalls significantly damage consumers’ confidence in the safety of their food and can lead to long-term avoidance of products that are directly or indirectly involved in recalls. Worse, these contaminated products are responsible for much of the foodborne illness that affects millions in the U.S. each year and results in total annual losses approaching $152 billion.

In the past year and a half there have been 728 market withdrawals, 77.7 percent of which were food recalls affecting consumers’ health. The 2006 U.S. E. coli spinach outbreak that occurred exemplifies the tremendous costs that a failure to identify, detect, and monitor pathogens can have on consumer
health and the economy. The outbreak resulted in 3 deaths and 205 confirmed illnesses, and reportedly affected 26 states. The $55 million spinach industry in Texas alone lost $11 million and resulted in the loss of 96 jobs. Similarly, a 2011 *E. coli* outbreak in Germany has caused 26 deaths and thousands of reported illnesses\(^1\). These costly outbreaks could easily have been detected and prevented by incorporating genotyping technologies into the food production system.

The same safety concerns hold true for the livestock industry. In April of 2010, an animal was diagnosed with foot and mouth disease in a small, isolated town on the Pacific coast of Japan. Within two months, 290,000 livestock would be culled resulting in an economic loss of over $3.14 billion—the worst epidemic ever to occur in Japan. A similar outbreak within the U.S. would cost over $700 billion and would cripple the U.S. livestock sector. However, the U.S. is not equipped to detect the introduction of an infected animal or prevent the spread of infection which leaves the livestock sector vulnerable.

Scrapie is a fatal, degenerative disease that affects sheep and is related to bovine spongiform encephalopathy (BSE or "mad cow disease"). It has the potential to pass to humans through the consumption of contaminated meat. Since the symptoms are subtle and diagnosis is difficult, transmission rates between sheep remain high, resulting in significant losses per infection. It is estimated that American sheep producers lose $25 million every year because of scrapie infections. Unfortunately, the most common detection method in the US involves an expensive, time-consuming labor-intensive biopsy test. The best initiative to preventing the spread of scrapie has been achieved in the UK through the use of genotyping technologies for screening infected sheep and by breeding scrapie-resistant sheep. Such methods were launched in 2001 with the National Scrapie Program (NSP), a strategic long-term plan that consists of a number of genotyping schemes. As a result of the NSP, scrapie cases have dramatically declined in UK. Because of the national implementation of these genotyping programs, it is estimated that within 10 years the prevalence of the most scrapie resistant trait will rise to 80 percent in the ram population and to 85 percent in the slaughter population.

Not all pathogen outbreaks affect consumer safety; often pathogens affect crop production, constraining industry producers. For example, in late 2009, the citrus industry in Florida was hit with a major Huanglongbing (HLB) outbreak, also known as citrus greening disease. To date, millions of citrus trees have been lost, putting the state’s $9.3 billion citrus industry and 76,000 jobs in jeopardy. While not harmful to consumers, HLB can decimate a grove and poses a serious threat to industry production. Since its arrival to the U.S. in 1998, it has become an immediate threat to the processing and fresh fruit industries in Florida, California, and Texas. Unfortunately, there is no cure for HLB and symptoms of infection are not immediately evident. Early detection is key to preventing the spread of the disease. Currently, the most common way to detect HLB is by regular visual inspection of each tree. However, this surveillance is time-consuming and inefficient. Furthermore, the latency and spread of HLB by flying insects makes its monitoring very difficult by visual inspection alone. By assaying whole groves of trees, diseased trees can be identified and quickly removed prior to development of visible symptoms so only a single tree is lost to the pathogen rather than a whole citrus grove that took multiple years to establish. Fast and high-throughput genotyping methods are required to prevent further destruction to the citrus industry.

All crops and animals are plagued by various microscopic pathogens. Widespread use of high-throughput multiplex genotyping technology could mitigate extensive crop damage and loss by early detection in all agricultural sectors and aid in more comprehensive bio-surveillance. Ideal pathogen detection in a sample identifies which pathogen is present, rules out the presence of other pathogens, identifies a specific variant that is present (e.g. H1N1 variant of the influenza virus), and determines the characteristics of a pathogen such as whether it carries any antibiotic resistance or any specific virulence traits. Genotyping technology can easily accomplish all these objectives rapidly for many samples simultaneously. The benefit of technology that can rapidly identify the pathogen and determine the appropriate treatment response cannot be understated. The ability to characterize a pathogen quickly for many samples is key to responding rapidly to contain disease transmission, whether in a farmer’s field, herd or during ongoing bio-surveillance.

High-profile cases of agricultural recalls have recently illustrated the economic importance of maintaining strong consumer confidence. For example, an 8-day recall of spinach products in California in 2006 resulted in a loss estimated between $37 and $74 million. However, this amount paled in comparison with the $350 million loss suffered by the industry the following year after sales dropped 20 percent below pre-recall levels, the result of reduced consumer confidence in the safety of spinach. Similarly, a 2007 FDA warning focused on salmonella-contaminated peanuts prompted a $78 million recall effort and the destruction of an estimated $1 billion worth of peanuts and peanut products. Sales of peanut butter products by the manufacturer initiating the recall fell by 63 percent soon afterwards. By making it faster and easier to isolate contaminated products at the earliest points of the supply chain, we believe the NAGC can help manufacturers avoid costly product recalls and provide a much-needed boost to consumer confidence in the safety of U.S. agricultural goods.

**Global competitiveness**

As the U.S. faces an increasingly competitive global marketplace for agricultural products, it's more important than ever for the nation to fully exploit its comparative advantages over other international exporters. As previously noted, many U.S. competitors have wisely shifted their agricultural focus towards products that play off of their greatest strengths. For example, Brazil, expecting to become the leading producer of soybeans and soybean products by 2020, has focused on its significant access to arable land. China, by comparison, continues to dominate the rice market and has proven a strong competitor in the production of fruits/vegetables (e.g. garlic, broccoli, lettuce, strawberries), thanks largely to its significant pool of low-cost labor. One of the most important ways the NAGC will improve U.S. competitiveness is by allowing the agricultural sector to better leverage two of its own fundamental strengths relative to its competitors, specifically, its technological prowess and world-class human expertise in research and development. By helping to unlock the value of the nation's technology and expertise, the NAGC will improve the agricultural sector's competitiveness in three key areas: productivity, product quality, and the rate of new product development.

---

2 Song et al. 2011, Deshpande et al. 2010
In an increasingly competitive market, one way the U.S. can preserve its strong position is by maintaining the exceptional quality and safety of its agricultural products. The importance of retaining agricultural product quality was recently highlighted by China’s food contamination crisis, which led to costly global recalls of many of its products and bans on the importation of certain Chinese goods by 20 countries. More recently, deaths in Europe linked to E. coli-contaminated vegetables have shaken confidence in the safety of German agricultural goods.

The NAGC would play a role in ensuring U.S. goods remain highly desirable in international markets in two ways. First, its previously described pathogen detection services would substantially improve biosurveillance efforts, reducing the incidence of high-profile quality-control problems that could damage the standing of U.S. agricultural products around the globe. Secondly, the NAGC will broaden industry's access to technologies that allow them to guarantee that their customers are receiving exactly the products they desire. For example, the European Union's new laws regarding mandatory labeling of genetically-modified foods could make it difficult for organic farmers to successfully sell their goods on European markets without independent confirmation that their goods are unmodified. While the U.S. has the genotyping technology to provide this confirmation, it may not be available to many who need it. The NAGC would fulfill that need.

Finally, the U.S.'s competitiveness is to some extent reliant on its ability to utilize the nation's expertise and technology to develop new products that the world needs in rapid fashion. Many traditional methods of selective breeding, though effective over long time scales, cannot possibly be used to develop products with the rapidity international markets demand. Marker-assisted selection (MAS) performed using genotyping, on the other hand, is rapid and cost-effective. By offering access to this technology at an affordable price, the NAGC will significantly accelerate the speed with which small, highly-innovative corporations are able to screen interesting genetic variants and develop new products that help ensure the US's agricultural portfolio remains competitive with those of other exporters.

Long-term agricultural projections for 2020 issued by the USDA Economic Research Service predict steady growth in crop and livestock demands, with increasing population and per capita income in many developing countries accounting for much of the increasing demand for soybeans, wheat, coarse grains, and beef. Although the U.S. is currently a leading exporter for many crops, it is expected to lose its market share due to a lack of investment in research infrastructure. U.S. wheat and corn exports are also expected to drop as exports from FSU (former Soviet Union), Brazil, China and Argentina rise. While emerging markets such as China and Brazil create stiff competition by relying on low-cost labor and expanding cultivated acreage, the U.S. will need to rely on technology to increase production.

Sean Gardner, Monsanto wheat business lead, said that high throughput genotyping and marker assisted selection, were critical components of Monsanto’s “basket of technologies” for wheat breeding.

www.agprofessional.com August 8, 2011
Both of these services will be available through the NAGC.
To maintain global competitiveness, efforts are focused on sustaining and increasing productivity through improved breeding schemes. Crop and livestock production has seen improvements through techniques that involve selecting plants or animals that carry desirable traits, referred to as marker-assisted selection. Indeed, continued technological and genetic developments is expected to increase milk production per cow by 85 percent or 3,525 more pounds of milk per dairy cow by 2020.

The beef and milk industry recognize the need for investment in genetic research. In 2009, the bovine genome was sequenced and paved the way for genotyping services to improve on current industry standards. The same year, the USDA funded a project to increase the understanding and use of MAS technology by beef cattle producers as these resources become increasingly available. For example, as more markers are identified, screening for genetic defects, carcass quality, fertility, yield, milk production and weight traits will have strong economic benefits for the industry.

Investment in the genomic era has generated a plethora of genetic markers associated with beneficial traits in both crops and livestock animals. The vast majority of these markers are under utilized due to a lack of available genotyping services. However, the use of DNA markers improves the efficiency and precision of conventional breeding and accelerates the development of agricultural crops with traits of interest by focusing breeding of individual plants with desired traits. Through genotyping, plants and animals with a trait of interest can be identified early in development before the trait may even be visible (for example, milk production, meat quality, or pathogen resistance). The genotyping services provided by the NAGC will make marker-assisted breeding and selection a reality to a much broader range of breeders across all of agriculture.

In recent years, other nations have demonstrated a significant willingness to invest in research infrastructure projects that may offer direct or indirect benefits to their institutions. For example, China's Beijing Genomics Institute (BGI), founded in 1999, now represents the world's premiere genome sequencing centers. In only a short time, BGI has sequenced or resequenced the genomes of many species relevant to agriculture, including: rice, chicken, silkworm, and cucumber. We anticipate that by focusing strongly on putting to use the high-throughput genotyping technology developed by LANL, the NAGC will greatly expand the nation's research infrastructure in ways that benefit many U.S. entities, in much the same way the BGI's emphasis on genome sequencing has expanded China's ability to rapidly sequence genomes of interest. We believe the NAGC would make the U.S. the leader in translating genomic information into products for agricultural problems.

**Bio-threats**

The U.S. agriculture and food industry is a $1 trillion economic sector and an integral part of every state’s economy. However, agriculture in the U.S. is dangerously fragile because of vulnerability to both natural outbreaks and deliberate disruptions. The vulnerability is a consequence of the concentrated and intensive nature of contemporary U.S. farming practices, which makes crops and livestock more susceptible to bio-terrorism. A major biological outbreak or attack would inflict a crippling blow to the U.S. economy. According to both U.S. and New Zealand experts, intentional introduction of foot-and-mouth disease (FMD), a potentially fatal viral disease that affects livestock like cattle, sheep and pigs, represents the most likely source of agricultural bioterrorism over the next

---

20 years. FMD could reach twenty-three states within five days if it is introduced into only one U.S. state. The estimated cost of a FMD attack in California alone for the first few weeks is between $6 and $13 billion\textsuperscript{6}. A major disease outbreak or bio-attack against the U.S. agricultural sector would disrupt the food supply and undermine consumer confidence. To ensure the safety and supply of livestock, the U.S. must actively monitor and survey the production of livestock.

Both the vulnerability of U.S. agriculture to bio-threats and the severe consequences associated with these threats suggest a need to evaluate and improve the existing response and surveillance strategies. The USDA Animal and Plant Health Inspection Service (APHIS) has protocols to respond to the unintentional introduction of plant and animal pests and pathogens, including border inspection, field surveillance and deploying first responders to deal with emergencies of both disease outbreaks and biological attacks. However, there is good reason to question whether our existing response capabilities can effectively deal with natural disease introductions. The U.S. is increasingly importing agricultural goods, yet less than one percent of more than 10 million imported entries are inspected annually\textsuperscript{7}. A high-throughput genotyping service is therefore needed to detect pests and pathogens at seaports and border crossing sites to counter agricultural outbreaks and bioterrorism.

Indeed, current laboratory and field resources are often strained when naturally occurring outbreaks occur. For example, university plant diagnostic clinics are typically understaffed and lack resources\textsuperscript{8}. In the event of a multifocal attack on agriculture, current resources are inadequate to respond to a high volume of new samples. Having a centralized and specialized detection laboratory would increase our capability to respond quickly and effectively to large disease outbreaks, whether the outbreak is intentional or unintentional.

If the U.S. is to ensure the security of its food, fiber and fuel supplies, productivity gains must continue to outpace growth in domestic demand for each of these agricultural outputs. By providing the U.S. agricultural sector with easy access to advanced genotyping services at low-cost, we believe the NAGC has the potential to significantly improve the security of food, fiber and fuel by enhancing U.S. productivity in all three of these areas. This expectation is supported to a significant degree by historical data. In fact, according to the USDA, the "unprecedented growth in agricultural productivity over the past century can be attributed largely to investments in agricultural research and technology development."\textsuperscript{9}

Though many factors have positively impacted food production in the U.S. in the last 100 years (e.g. more efficient machinery, better chemicals and fertilizers, changes in farm management approaches), the genetic improvement of crops and livestock has clearly been one of the most significant. Because the NAGC will provide cost-effective genotyping services to those involved in marker-assisted breeding efforts, we believe the magnitude of its future impact on food production and security can be illustrated by comparing sectors where genetic screening and trait selection are widely utilized with those where they are not. For example, genetic improvements in American Holstein dairy cattle have led to tremendous gains in productivity over time (a tripling of milk production despite a two-

\textsuperscript{6} Polyak, M. G. The Threat of Agroterrorism, Summer/Fall 2004.
\textsuperscript{7} Globalization Exposes Food Supply to Unsanitary Practices, May 2011.
\textsuperscript{9} http://www.ers.usda.gov/Briefing/AgResearch/background.htm
thirds reduction the number of cows), while the beef cattle industry (which has not utilized the same structured improvements in genetics) has not witnessed the same gains.\textsuperscript{10} The NAGC will make such selective breeding efforts \textit{throughout the U.S. agricultural sector} faster, cheaper, and more effective, leading to the productivity gains the country requires to ensure the security of its food supply going forward.

\textbf{Fiber security}

The global demand for fibers has seen steady increases pressuring producers to develop improved breeding strategies to meet projected demands for cotton, wool and wood fibers, which are among the most important natural fibers in the world. In 2010, cotton consumption rose by 3 percent, while wool demands increased by 5 percent\textsuperscript{11}. The bio-renewable fuels market will surge wood fibers demand from 2 million tons to at least 13.5 million tons by 2020\textsuperscript{12}. In the future, world income and population growth will stimulate a 4.5 billion pound increase in global fiber demand each year\textsuperscript{13}. However, at currently estimated growth rates, the production of both man-made fibers and natural fibers will not be able to meet future global fiber demand\textsuperscript{14}. Fortunately, the application of genomic information will enable us to overcome this challenge by helping producers maximize their yields.

Genotyping can be used to increase the quality and yield of fibers by expediting the identification of the desirable quality and yield traits of cotton, and the incorporation of these traits into a single genotype to create the ideal cultivar\textsuperscript{15}. For example, genomic technologies will facilitate the development of drought-resistant strains to overcome potential water scarcity and uncertain climate changes. Cotton provides a good example in this regard. This fiber is the single most important textile fiber in the world, but is highly susceptible to attack from pests (e.g. cotton bollworm) and has substantial water requirements. Genetically modified cotton, by comparison, is engineered to be pest- and drought-resistant, and represents 93\% of cotton grown in the US\textsuperscript{16}. Because cotton production is water intensive, U.S. cotton production is expected to decrease 0.6\% in 2011/12 because of a range of adverse growing conditions, including droughts in Texas, floods in the Mid-South, and dry conditions in the Southeast\textsuperscript{17}. The development of drought-resistant cotton would mitigate these loses. Seed-developer Monsanto has been developing a drought-resistant genetically modified cotton strain. However, it is expected to be released for commercial cultivation until 2015\textsuperscript{18}. Access to cost-effective genotyping for industry researchers will expedite such crop innovations and importantly, will cut research costs, savings that will be transferred to growers.

In a world where the environmental challenges facing farmers are escalating, the need has never been greater for genotyping services that guarantee a farmer’s seeds carry the traits that make them

\textsuperscript{11} A Quarterly Insight into the U.S. and Global Wool Market. Wool Journal, March 2011
\textsuperscript{12} Quantifying Forest Biomass Resources in the U.S. South Forest2Market, Aug. 2008.
\textsuperscript{13} http://www.cottoncampus.org/Cotton-Environmentally-Friendly-Sustainability/
\textsuperscript{14} Global textile sector to run short of fiber – Report Gherzi Textil Organisation AG , Feb. 2011 (Source: Fibre2fashion)
\textsuperscript{16} National Agricultural Statistics Board Annual Report; June 30, 2010.
\textsuperscript{17} U.S. Cotton Market Monthly Economic Letter Cotton Incorporate, May 2011.
\textsuperscript{18} Monsanto develops drought resistant genetically modified cotton CropBiotech Update, April 2007.
resistant to these challenges. By providing access to such services, the NAGC will play a crucial role in ensuring the nation maintains strong, secure supplies of cotton and other key fibers.

**Cellulosic renewable fuel**

A number of policy incentives have been set in place to meet future energy demands. For example, the 2007 Energy Independent and Security Act required the use of 9 billion gallons of renewable fuels in 2008, increasing each year to 36 billion gallons by 2022. Bio-renewable fuel, produced from lignocellulose using non-edible plant sources, such as corn stover, grasses, and wood is a subject of intense study and in the early stages of development. Lignocellulose is a complex structural component that comprises much of a plant's mass and is used to produce fuel ethanol by fermentation. Since lignocellulose is the component that gives a plant its robust structural integrity, breaking it down is a costly and energy-intensive process, making up a large fraction of the production cost.

Genomics research focused on engineering improved non-edible plant-based fuel sources is understood to be a critical component to meeting future energy needs. Currently, efforts are focused on sequencing the genome of energy crops and identifying the genes that regulate lignocellulose formation, a subject that has received little attention until now. Today, 235 million metric tons of corn stover (stalks, leaves, cobs, husks, and tassels) is left un-harvested each year. Corn hybrids used today have been bred for grain yield, but research into stover-quality markers will be useful in the conversion of the non-edible parts of the plant into bio-renewable fuel. Supporting these efforts through additional genotyping resources will undoubtedly bring us closer to new and improved fuel resources.

Given that the use of bio-renewable fuels is on the rise in the U.S. and around the world, the relevance of these energy sources to the security of the nation's fuel supply is on the rise as well. The NAGC anticipates playing an important role in the production of existing biorenewable fuels and the development of new ones by making it easier and more cost-effective to assay the biological inputs used in fuel production. For example, the Center would allow researchers searching for new strains of algae (whose lipids/oils offer significant promise as biorenewable fuel sources) to easily assay environmental samples for genes of interest that might indicate strong fuel production profiles. Similar assays could be applied to any species believed to have promise in biorenewable fuel production, accelerating the development of the most eco-friendly and economically viable fuels, thus strengthening national fuel security and reducing our dependence on fossil fuels.

**Lack of genotyping access**

The ability to detect and monitor pathogens, and to identify genetic traits is critical to the agricultural sector in ensuring consumption safety, protecting producers, and increasing production levels. Resources currently available in the U.S. to meet this genotyping need, however, are fragmented and grossly inadequate, significantly limiting the accessibility to agricultural genotyping. Most high throughput genotyping services are currently provided by large biotechnology companies but remain highly institutional and limited to internal use. Other available services on the market usually focus on

---

one narrow field, such as one disease or one breeding selection. These services typically use outdated, slow, and expensive technologies. To the many food producers or consumers, this makes the genotyping solution, though very effective, less accessible and economically unappealing.

In addition, existing genotyping centers associated with government, state, and academic organizations are unable to respond to the national demand. Often, thousands of samples must be screened to effectively mitigate the spread of pathogens, and most genotyping services lack the capacity to analyze such high volumes. Furthermore, the technologies behind these services are not flexible enough to address novel challenges, such as previously unidentified pathogens or genetic markers. The solutions to those challenges require a technological platform that is fast, adaptable, and high-throughput. Given the importance of agriculture to the U.S., a centralized, efficient, freestanding, and economic agricultural genotyping center is needed.

IV. Increasing Agricultural Research Infrastructure and New Technology

The National Corn Growers Association and Danforth Plant Science Center are partnering with Los Alamos National Laboratory (LANL) to create the National Agricultural Genotyping Center (NAGC). LANL will provide new technology and bioinformatics to the NAGC and conversely the NAGC will be a conduit for LANL developed technologies into the agricultural industry.

LANL developed MOL-PCR high-throughput genotyping platform

The NAGC is partnered with LANL, the premier research institution in the world with a proven track record in developing high-throughput genotyping technology. LANL has developed a multiplex genotyping technology strategy for the Department of Homeland Security which was adopted by the Centers for Disease Control and Prevention. The NAGC is licensed to utilize the LANL patented genotyping technology for the agricultural sector, to use existing assays and to develop new assays to suit specific customer needs. Specifically, the LANL technology is a multiplex genotyping technology called Multiplex Oligonucleotide Ligation – Polymerase Chain Reaction (MOL-PCR).

The LANL MOL-PCR multiplex technology is high-throughput, fast, cost-effective, specific for traits of interest, and customizable. The multiplex nature of the MOL-PCR technology allows 2-500 genotyping markers (unique DNA sequences) to be tested per sample, which employs a rapid and cost-efficient method to survey many markers and many biologic samples simultaneously. A single MOL-PCR assay is completed in only 4 hours and provides information on up to 125 times more traits at a cost 25 times less than competitor technology. In a single week, two assay machines could provide up to 15 million data points compared to only 129,000 data points from competitor technology. In an example where a customer may want to test 10,000 samples for 50 markers, corresponding to 500,000 datapoints, the MOL-PCR technology saves $115,500 and approximately 50 days over similar technologies (Table 1).
Table 1: Costs and savings for analysis of 50 markers for 10,000 samples.

<table>
<thead>
<tr>
<th></th>
<th>MOL-PCR</th>
<th>Current technology</th>
<th>MOL-PCR savings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td>$9,500</td>
<td>$125,000</td>
<td>$115,500</td>
</tr>
<tr>
<td>Time (in hours)</td>
<td>104</td>
<td>1302</td>
<td>1198</td>
</tr>
<tr>
<td>Time (in days)</td>
<td>4</td>
<td>54</td>
<td>50</td>
</tr>
</tbody>
</table>

This technology has been developed to identify the human pathogens: *Bacillus anthracis*, *Yersinia pestis*, and *Francisella tularensis* in clinical samples as well as for detection of the citrus pathogens, *Candidatus Liberibacter* spp. As additional crops, pathogens or resistance genes are desired to be assayed, additional markers can be developed to allow assay customization to meet customer needs. Stringent bioinformatic tools and quality control assays have been developed by LANL to facilitate marker development to ensure that specific, accurate results will be delivered even when a large number of markers are used simultaneously. Once markers are established, the markers are available for repeated use for both current and new customers. For the growing market of customers that need genotyping of a large number of markers, MOL-PCR provides a fast, high-throughput, cost-effective and customizable alternative to current available technologies.

Los Alamos National Laboratory has considerable experience in the design and testing of nucleic acid assays for the detection of human, animal and plant pathogens. The main funding for this work has come from the Department of Homeland Security (DHS), and a number of LANL assay designs have been transitioned by the DHS for use at the Centers for Disease Control and Prevention (CDC). Other support has come from the Citrus Research Board and from private industry. Over the past 10 years, LANL has designed assays for all of the key biothreat and public defense viral and bacterial pathogens.

The design methods employed at LANL rely extensively on computational techniques for genome comparison that were developed at LANL for the DHS and that are implemented on a large dedicated cluster of high performance computers. These methods are ahead of the current state of the art and allow LANL to identify assay designs that cannot be achieved elsewhere. The computational methods developed at LANL are applicable to any of the existing hybridization-based nucleic-acid assay methods (PCR, TaqMan, microarrays, NASBA, etc). However, in addition, LANL has considerable unique expertise with the MOL-PCR platform that will be deployed by this initiative. Tools have been developed and continue to be improved that are specific for MOL-PCR assay designs.

LANL will be responsible for the bioinformatics component of this initiative. Their work will be primarily focused on the design of nucleic acid assays. Additional tasks may involve sequence analysis for improved understanding of assay performance, database support, and support for development of counter-measures. Research needed to maintain state of the art capabilities may also be necessary.

**Other genotyping platforms**

The NAGC will offer other genotyping platforms including but not limited to

- Taqman
- RT-PCR (qPCR)
- Sequencing
- SSR
- ELISA
- Microarray
- Discovery sequencing at LANL’s high-throughput sequencing center

**NAGC Customers**
The NAGC will focus primarily on providing genotyping services to agricultural customers that include agricultural researchers in academia and private industry as well as state and federal government agencies and the food industry (Table 2). The NAGC will be particularly suited for customers who need high-throughput genotyping to screen multiple markers per sample. In this specialized capacity, the genotyping service of the NAGC will serve as an affordable resource for many customers and states that do not have the infrastructure for a similar genotyping lab. The goal of NAGC will be to provide a cost-effective genotyping service that specializes in pathogen detection and facilitation of marker-assisted breeding and selection, across the nation to a broad spectrum of crops and animals.

**Table 2. Potential customers of NAGC**

<table>
<thead>
<tr>
<th>Sector</th>
<th>Customer</th>
<th>Needs</th>
<th>Can the NGC address need?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Government</td>
<td>USDA</td>
<td>Identify contaminated food products or diseased crops</td>
<td>Yes</td>
</tr>
<tr>
<td>Government</td>
<td>Fish &amp; Wildlife Service</td>
<td>Monitor natural populations for disease presence or test samples in case of outbreak i.e. bird samples during avian flu</td>
<td>Yes</td>
</tr>
<tr>
<td>Government</td>
<td>DHS</td>
<td>Agrosecurity surveillance to protect food and other agricultural supplies</td>
<td>Yes</td>
</tr>
<tr>
<td>Government</td>
<td>EPA</td>
<td>Monitoring environment, and safeguarding potential threats, diagnostic testing</td>
<td>Yes</td>
</tr>
<tr>
<td>Government</td>
<td>State Emergency Response Commission</td>
<td>Detection and diagnostic needs of potential biotic hazards</td>
<td>Yes</td>
</tr>
<tr>
<td>Government</td>
<td>Department of Health</td>
<td>Detection and diagnostic needs of potential pathogens</td>
<td>Yes</td>
</tr>
<tr>
<td>Government</td>
<td>Law Enforcement agencies</td>
<td>Assistance in forensics diagnostics and detection</td>
<td>Yes</td>
</tr>
<tr>
<td>Academic</td>
<td>Any college or university</td>
<td>Access to genotyping for research to improve agricultural crops</td>
<td>Yes</td>
</tr>
<tr>
<td>Private</td>
<td>Any ag company</td>
<td>Quickly and efficiently identify plants &amp; animals with traits of interest for breeding</td>
<td>Yes</td>
</tr>
<tr>
<td>Individuals</td>
<td>Veterinarians</td>
<td>Test animals for disease presence</td>
<td>Yes</td>
</tr>
<tr>
<td>Individuals</td>
<td>Farmers</td>
<td>Check crop pedigree, presence of traits of interest, determine parentage of animals</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**Business model**
Founded as a 501(c)(3) organization under the IRS tax code, the NAGC will be self-sustaining in five years. The specialized high-throughput genotyping service is expected to generate enough revenue to cover operating costs and provide investment capital. As a not-for-profit institute, the NAGC will provide independent, third-party results and will not be run by a government agency, private company or individual breeder. Results will be robust, accurate and fully disclosed. The NAGC will meet the national need for affordable genotyping across all agricultural crops for both pathogen detection and crop improvement.
Initial start-up funding is being sought to initiate and sustain the operation of the NAGC for the first five years. The anticipated start-up funds are $5 million upfront with an additional $15-20 million over a 5-year period. The start-up funds will provide resources to lease laboratory and office space according to the market rate in the St. Louis, MO area, hire researchers, technicians and other essential staff, and will finance the initial purchase of equipment for an initial maximum processing capacity of 400,000 samples per week. The start-up funds are crucial for the initial growth phase of the NAGC.

V. Executing on the Plan

“But instead of building separate and duplicative resources agency by agency, state by state, university by university, we should identify which agencies, departments and institutions have the critical skills to solve a problem and focus that combined knowledge and capacity where it will do the most good,”

Catherine Woteki, USDA Under Secretary for Research, Education & Economics.

NAGC Partners
The National Agricultural Genotyping Center is supported through a partnership with leading research and trade organizations including the Los Alamos National Laboratory, the National Corn Growers Association, and the Donald Danforth Plant Science Center, a global leader in plant research. The Los Alamos National Laboratory (LANL), the premiere research institution in the world, will provide the technological and informatics expertise to maintain advancements in MOL-PCR, which will ensure the diverse need for genotyping, is met. The LANL research team responsible for developing the unique genotyping platform has over two decades of extensive genotyping research experience and will be an integral part of ongoing tech development efforts at the NAGC. Through this partnership, the NAGC will remain the leader in large-scale genotyping and provide innovative solutions to the plethora of genotyping needs. Furthermore, the LANL has partnered with research institutions across the world to develop assays for detecting novel pathogen threats in foreign environments. This assay development will ensure the NAGC will be prepared to detect and identify completely novel pathogens never seen within U.S. borders. In order to maintain close ties to the agriculture sector, the NAGC has partnered with the National Corn Growers Association (NCGA). The NAGC will benefit from this partnership by maintaining a direct link with the agricultural producers. NCGA represents 35,000 dues-paying corn farmers nationwide and the interests of more than 300,000 growers who contribute through corn checkoff programs. A partnership with the NCGA will facilitate access to farmers in 48 states. Finally, the NGC has full support from the Donald Danforth Plant Science Center (DDPSC) to further provide research expertise, administrative and operation support, and advising oversight. A partnership with the DDPSC will provide a rich, collaborative research environment and access to over 170 leading scientists.

NAGC Leadership
Experienced scientists and industry leaders in agriculture genotyping and plant research will direct the NAGC. A Laboratory Director will be hired to manage operations and report to a board of directors who will provide oversight for NAGC activities.
**NAGC Location**

“St. Louis, unlike other competitor plant and life science regions, has an established leadership position in biomedical-related research and development, plant science, and agriculture-related biotechnology research and development upon which to build a highly robust and diversified plant and life sciences industry base.”

*Battelle Memorial Institute*

As a global center for agriculture research and production, St. Louis, MO provides the perfect location for the NAGC to set up operations. St. Louis boasts a vibrant agricultural industry with nearly 400 plant and life sciences companies, a dynamic academic research environment with the world’s largest concentration of plant science PhDs, and the presence of several large trade and agricultural organizations. The NAGC will benefit from industry connections with prominent St. Louis biotech and life science corporations like Monsanto, Covidien, Sigma Aldrich, Bunge North America, and Solae. Close proximity to industry leaders will create innovative collaborations and commercial opportunities. The NAGC will also have the opportunity to develop close scientific and technical relationships with expert plant and genetics scientists including researchers at the University of Missouri System, Saint Louis University, Missouri Botanical Garden, Washington University in St. Louis, and the Genome Institute, who was responsible for successfully sequencing the Maize genome. Further cooperative relationships with national stakeholders like the National Corn Growers Association, the American Soybean Association, the U.S. Farmers & Rancher Alliance, and the World Agriculture Forum, whose headquarters are all located in St. Louis, will enhance the NAGC’s national presence. Its central location within the U.S. means easy engagement for agricultural producers who will utilize the NAGC services. Indeed, 50 percent of the nation’s farmland lies within a 500-mile radius of St. Louis. The NAGC will also benefit from its proximity to the newly established USDA Statistics Center by being sensitive to agriculture trends and expectations.

As a member of the St. Louis community, the NAGC will provide new competencies to St. Louis start-ups and will actively contribute to the training and professional development of young scientists. NAGC sponsored engagement programs with local colleges and universities will provide young scientists with direct exposure to the commercial application of biotechnology and instill in them a spirit of entrepreneurship.

**NAGC Facilities**

The NAGC will be housed via a lease in the Bio Research & Development Growth (BRDG) Park at the DDPSC. BRDG Park, whose mission is to help companies transition from an idea or concept to a commercially viable product, is uniquely positioned to house the NAGC and provide on-site expertise in commercial and research development. As an extension of the Danforth Plant Science Center, the BRDG Park fosters a spirit of collaboration among its tenants. Being part of the BRDG Park will grant the NAGC access to the intellectual capital of the DDPSC, the world’s largest independent research institute focused on plant science, as well as state-of-the-art facilities.
VI. Impacting the Industry and the Nation

“My response to this trying U.S. budget situation is to keep pointing out to all the audiences I speak to that investing in agricultural research is an investment for everybody. I talk first about the payoff for farmers, in new technology that they can use to increase their productivity and reduce their costs. But that also pays off for the general public in a wider variety of foods available and in reasonable food prices.”

Catherine Woteki, USDA Under Secretary for Research, Education & Economics.

Job creation and workforce development
The NAGC will serve as an engine of job creation and workforce development in the St. Louis region. In its first year of operation, 12-15 high-paying positions will be created for staff scientists, research technicians, and administrators. In subsequent years, as service volumes increase and the client base expands, the NAGC workforce is expected to grow beyond 50 employees. Further job creation outside the confines of the Center is anticipated as spin-off companies are established to commercialize NAGC technologies and research. Further, we expect that the significant concentration of skills and expertise encompassed in the NAGC's employees will be harnessed for workforce development initiatives in surrounding biotech startups. Given these many benefits, the impact of the NAGC on the employment landscape in St. Louis is expected to be overwhelmingly positive.

Expanded access to services
Though affordable genotyping has the potential to benefit many in the U.S. agricultural sector, most do not currently enjoy access to this important molecular tool. The NAGC will augment the nation's research infrastructure and genotyping capacity, increasing the availability of cutting-edge genotyping services for many different parties. Further, NAGC's superior technology will allow it to guarantee substantial cost savings, significant efficiency improvements, and shortened turnaround times for its customers.

Corporations' access to genotyping technology is largely dictated by their size. While large agribusinesses (e.g. Monsanto, DuPont) have staff and equipment dedicated to genotyping, smaller companies typically do not. The NAGC will offer genotyping at a price point that is competitive with, or superior to, the assays performed by the largest corporations. Access to this service will give small, nimble firms a greater opportunity to innovate while providing large firms with an opportunity to cut R&D costs and improve the effectiveness of their selective breeding programs (via reduced turnaround times).

Sole proprietors in the agricultural sector (e.g. farmers, independent breeders, veterinarians) currently have very little if any access to affordable agricultural genotyping services. The NAGC will meet this need and offer these individuals many valuable services, including the ability to evaluate the pedigree/paternity of livestock (when bred off-site or through artificial insemination), verify lineage purity, and test for disease susceptibility. Additionally, the NAGC will offer inexpensive seed trait verification, a service which is rarely available to the U.S. farmer.

Many government agencies (incl. USDA, FDA, DHS, EPA, USF&W) also stand to benefit a great deal from the NAGC's significant genotyping capacity. Partnering with the NAGC will grant many agencies
the ability to address important questions they simply do not have the resources to tackle at present. In today's challenging budget climate, project cost containment is more important than ever. Fortunately, the cost-effectiveness of MOL-PCR's multiplexing approach will also ensure that state and federal agencies can also accomplish more with less funding by utilizing the NAGC.
NAGC Partners

The National Agricultural Genotyping Center is supported through a public and private partnership of leading research and trade organizations including Los Alamos National Laboratory, National Corn Growers Association, and Donald Danforth Plant Science Center. The Los Alamos National Laboratory (LANL) will provide the technological and informatics expertises to maintain technological advancements and ensure diverse genotyping needs are met. In order to maintain close ties to the agriculture sector, the NAGC has partnered with the National Corn Growers Association (NCGA). NCGA represents 35,000 dues-paying corn farmers from 47 states and the interests of more than 300,000 growers who contribute through corn checkoff programs. The NAGC has full support from the Donald Danforth Plant Science Center to further provide research expertise, administrative and operation support, and advising oversight. This partnership with the Danforth Center will provide a rich, collaborative research environment and access to over 170 leading plant scientists. The NAGC also will forge partnerships with land-grant universities, non land-grants universities, government agencies and industry.

genotypingcenter.com

Dr. Richard Vierling • vierling@ncga.com • (636) 733-9004
Sam Fiorello • sjfiorello@danforthcenter.org • (314) 587-1011
Dr. Scott White • scott_white@lanl.gov