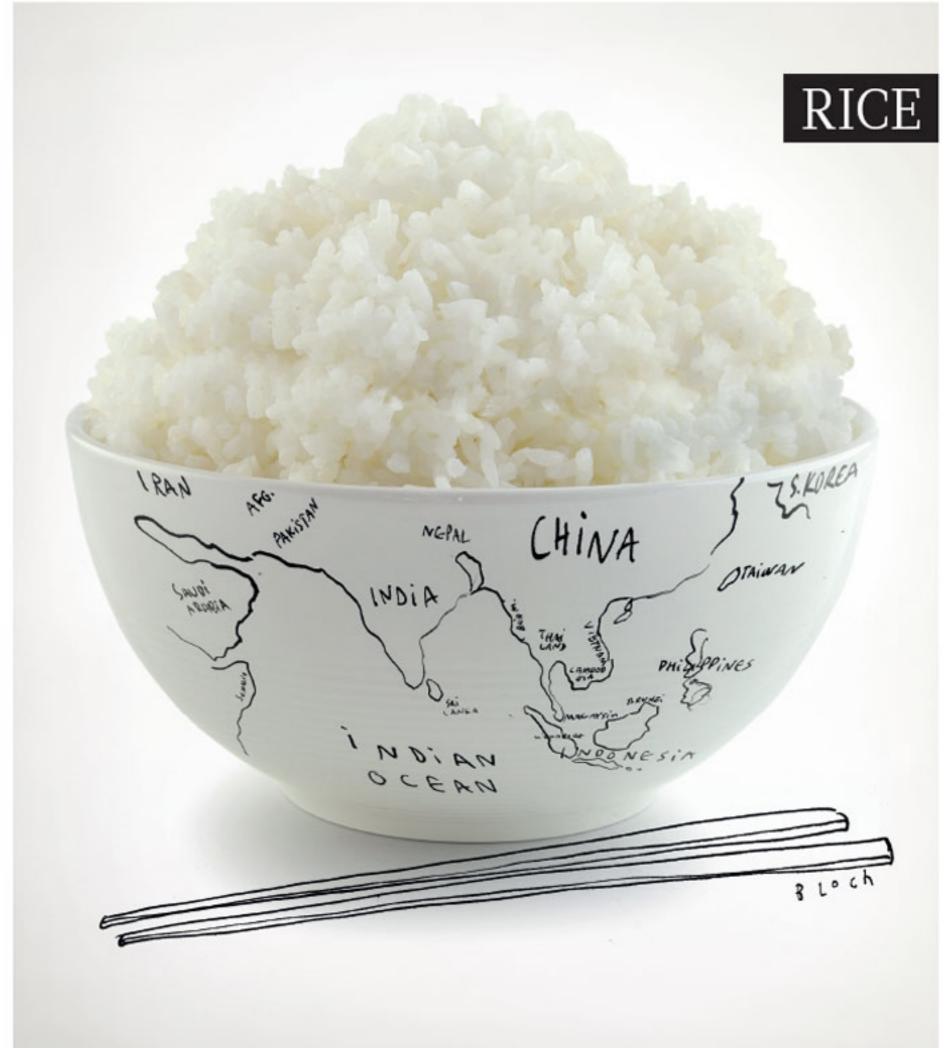
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New thinking about an old grain

natureoutlook RICE

30 October 2014 / Vol 514 / Issue No 7524



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Editor-in-Chief Philip Campbell R ice is not just another grain. For three billion people, it is a daily necessity (page S50). Since its domestication some 8,000 years ago (S58), rice has played a part in building civilizations, shaping societies and, most of all, feeding a growing world.

But the climate is changing, and much of the land that once went to paddies is being consumed by expanding cities. There is a realization that farmers cannot keep applying fertilizers and pesticides to their crops without environmental consequences. If rice is going to feed future populations — in Asia, Africa (S64) and beyond — scientists will have to help to improve yields.

Rice research involves scientists around the world. This year marked a milestone achievement: the publication of the genomes of 3,000 strains of rice will help to guide the creation of hardier, more productive crops (S60). Researchers are addressing a massive nutritional crisis by converting rice into a vehicle for vitamin A, but a combination of technical challenges and public opposition threatens the development of this 'golden' rice (S55). Scientists plan to retool the way in which rice harvests energy from the Sun (S52) and are tackling problems such as arsenic contamination (S62).

Many questions remain, but the biggest — will there be enough rice? — will take decades to decide. Governments and scientists can use that time to work together on the answer (S66).

We are pleased to acknowledge the financial support of the Institute of Genetics and Developmental Biology, Chinese Academy of Sciences (CAS); the Institute of Plant Physiology & Ecology, Shanghai Institutes for Biological Sciences, CAS; the Institute of Botany, CAS; the Institute of Crop Science, Chinese Academy of Agricultural Sciences (CAAS); and the China National Rice Research Institute, CAAS, in producing this Outlook. As always, *Nature* has sole responsibility for all editorial content.

Chris Woolston *Contributing Editor*

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CITING THE OUTLOOK

Cite as a supplement to *Nature*, for example, Nature **Vol. XXX**, No. XXXX Suppl., Sxx–Sxx (2014).

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The Nature Outlook Rice supplement can be found at http://www.nature.com/nature/outlook/rice

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A GOOD GRAIN

Millions of people around the world rely on rice as the bulk of their daily diet. This snapshot of the crop's production, consumption and trade shows an overall surplus, but population growth in future decades may affect the situation, writes Emily Elert. 2011 90

DAILY DEPENDENCE

Average percentage of daily calories derived from rice 1961-2011, per capita. Factors that affect the demand of rice include: rapid economic development: increased gross domestic product; and urbanization in developing countries.



Region with the largest continued reliance on rice for average daily calories: ASIA



Country with the largest continued reliance on rice for average daily calories: BANGLADESH



Country with the largest drop in reliance on rice for average daily calories: THAILAND





Country with the largest increase in reliance on rice for average daily calories: GUINEA

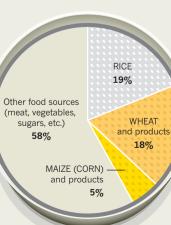


OCEANIA

GLOBAL NUTRITION

On average, every day, each person on the planet consumes:

42% of our daily energy supply comes from cereal crops (rice, wheat and maize).



INCREASED DEMAND

Population,

billions of people

2007

1991 1990 1989 1988 1987 1986

Global Developed countries

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60

50

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1961 1962 1963 1964 1965

Daily energy supply, kcal/person/day

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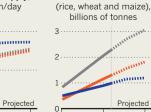
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2050

1961

2007

Developing countries



2007

2050

Production of cereals

1970 1971

1972

1973

1974

1975

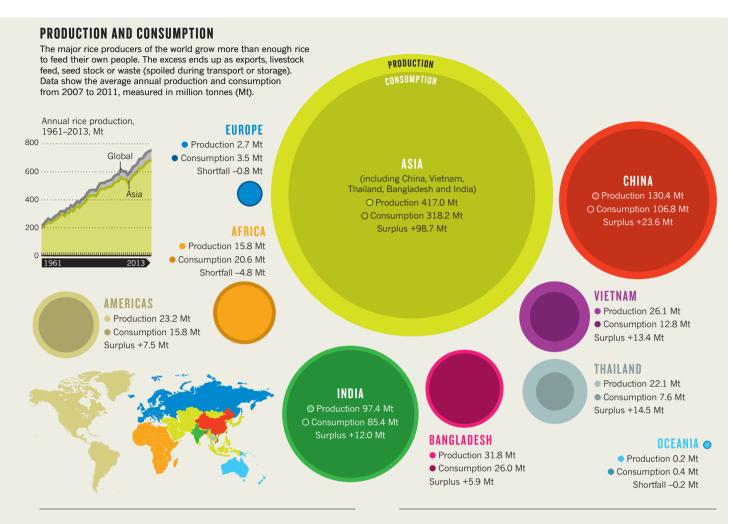
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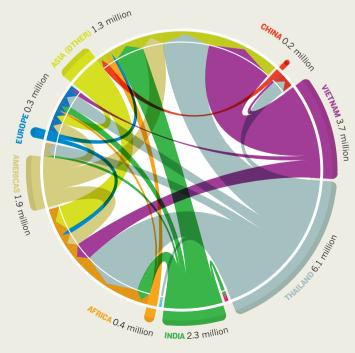
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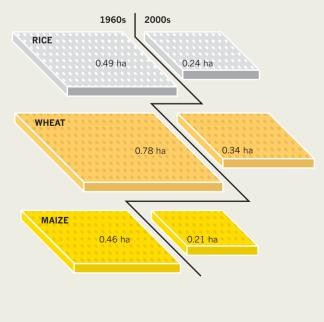
IMPORTS AND EXPORTS

Most rice is consumed in the country where it is grown, but increasing demand in Africa has lead to broader global trade. Data show the average annual export amount in tonnes from 2007 to 2011.



SPACE TO GROW

Improved rice strains and modern agricultural techniques have meant that farmers can produce higher yields on a smaller area of land. The figure shows the average area of land needed to produce 1 tonne.



Data source: Food and Agriculture Organization of The United Nations, Statistics Division.



Rice is a staple food, but production is not keeping pace with the rise in global population. So scientists are dreaming big and aiming high to change the future for this crucial grain.

BY LEIGH DAYTON

esearchers looking for the next big thing in rice studies have to deal with all sorts of obstacles, including, surprisingly, salt-water crocodiles. The swathes of wild rice growing in the tropics of northern Australia are thought to harbour game-changing genetics, but they also keep some unpleasant company. "It is a little bit tense," confesses Robert Henry, a plant geneticist at the University of Queensland in Brisbane, Australia, who is also director of the University's Queensland Alliance for Agriculture and Food Innovation. "The crocs might explain why the rice is under-studied."

For Henry and his colleagues, Australia's wild rice is a potential treasure trove, a source of ancient genetic diversity that could hold the key to protecting rice crops worldwide from a fungal disease that happens to be one of rice's biggest natural enemies. The team is not alone in going beyond the basic nuts and bolts of rice research. Worldwide, researchers increasingly recognize that wholesale application of fertilizers, bombardment with fungicides and other conventional approaches to creating bigger, better rice plants are so last century. "We need another green revolution to meet demands for food," says Robert Furbank, a plant physiologist food," says Robert Furbank, a plant physiologist $_{\overline{5}}$ with the Commonwealth Scientific and Industrial Organisation (CSIRO) near Canberra.

Not only are these rice researchers calling for $\frac{1}{2}$ revolution, they are working on one. They are applying the tools of genetics, bioinformatics, plant physiology and even evolution to the task. Plant geneticist Allen Good at the University of Alberta in Canada says that they are thinking visionary science and betting on high-risk research that may or may not pay off, but if it does, it would be, well, revolutionary.

It is definitely time for big ideas. Rice is a world staple, but production is struggling to keep pace with population growth. The agricultural system itself is in peril; climate scientists warn that the shift in the planet's weather systems will make clean water - the stuff of life for rice — increasingly scarce. Sea-level rise is already increasing rice-killing salinity in the deltas of Asian rivers, the richest rice-growing areas of the world. Added to these pressures is the fact that, worldwide, agricultural land is being converted to housing or industrial uses at a breakneck pace.

As Furbank notes, science has come to the rescue before. The first green revolution - conceptually kick-started in the 1940s and 1950s by the late US plant scientist Norman Borlaug and Indian rice geneticist M. S. Swaminathan, founder of the M. S. Swaminathan Research Foundation — delivered higher-yielding strains of rice through selective breeding for useful traits such as plant size and productivity. Combined with public policies that promoted farmer training programmes in developing nations and the widespread application of artificial nitrogen fertilizer, the improved strains doubled wheat and rice yield in Asia and Latin America in the 1960s and 1970s.

So in laboratories, fields and wetlands around the world, teams of scientists are tackling the big challenges of rice research: novel ways to exploit the energy of the Sun; new technologies to help rice plants to kick the fertilizer habit and feed themselves; and dramatically improved resistance against devastating diseases.

PHOTOSYNTHESIS SHIFT

The big idea started over a few beers in the early 1960s. At the time, Australian scientists Hal Hatch and Roger Slack were both employed in the laboratory of the Colonial Sugar Refining Company in Brisbane. The pub-time conversation got around to a mutual curiosity: how did the cane plant produce and store so much sugar? While investigating this seemingly simple question, they made one of the most important discoveries in the history of plant science: the C₄ photosynthetic pathway¹. This is the process by which cane and nearly one-fifth of all plant species convert inorganic carbon dioxide from the air into an organic compound, sugar (see 'Photosynthesis variants').

The C₄ pathway is more efficient than the alternative C₃ pathway — well-known to Hatch

and Slack — because it wastes less light energy when fixing CO_2 . And as an added benefit, C_4 plants need less water and nitrogen to fuel the process. In short, C_4 plants do more with less. The C_4 pathway was later found in other crop plants, including maize (corn), millet and sorghum — but not rice.

Scientists reasoned that if they could turn C_3 rice into C_4 rice, more of the crop could be produced, and produced more sustainably, even in a hotter, dryer, more crowded world. The International C_4 Rice Consortium (ICRC), headquartered at the International Rice Research Institute (IRRI) in Los Baños, the Philippines, estimates that the supercharged rice could support yield increases of a remarkable 30–50% with the same amount of water and fertilizer used on current C_3 crops.

As pointed out in 2013 by John Sheehy, former head of the Applied Photosynthesis and Systems Modeling Laboratory at IRRI and the father of the institute's C_4 project, the conversion from C_3 to C_4 occurred in evolution multiple times in the past 60 million years in plants growing in warm, semi-arid regions of the planet. Because rice can thrive in such climates, it is seen to be a good candidate. Sheehy notes that they are imitating nature, not inventing something from scratch.

Still it is not an easy task. "Owing to complex changes associated with C4 photosynthesis, it is no understatement to define this conversion as one of the grand challenges for biology in the twenty-first century," write Sarah Covshoff and Julian Hibberd, scientists at the University of Cambridge, UK². Fortunately, this was recognized early on, not just by Sheehy but by the US-based Bill & Melinda Gates Foundation. To understand the foundation's part in the process, it is necessary to turn the clock back seven years. It was after inviting global experts, including Furbank and Hibberd, to a workshop in 2007 that Sheehy took a group of scientists and a proposal to the philanthropic foundation. The result was a US\$20-million grant and establishment of the ICRC in 2008. Today, 22 teams from 9 nations collaborate on different aspects of the endeavour. "The project aims to enhance photosynthesis in crops like rice and wheat by giving them the genes that allow crops like maize to be so much more productive," says plant physiologist Paul Quick, who took over as project leader in 2009 when Sheehy retired.

According to Quick, there are two key components of the project. First, the identification and introduction of C_4 genes into C_3 plants. "We've already added 6 of the 12 genes we think are necessary," he says. The second involves changing the anatomy of the rice leaf to introduce specialized cells that allow the plant to break down CO_2 in the absence of oxygen, making the process more efficient. Unfortunately, the researchers do not yet know the underlying genetics for this stage. "So we have a gene-discovery programme that uses bioinformatics and mutagenesis to identify those genes," says Quick. A number of candidate genes are currently being put through



Rice blast disease can decrease yield.

their biochemical and anatomical paces.

What is the timeline for seeing the first crop of C_4 rice planted? Furbank says he expects a prototype crop within three years, but his best guess is that it will take another 15 years before C_4 rice is ready for cultivation in farmers' fields.

DIY FERTILIZER

Rice research is usually associated with yearround warm climates, so an institute in Alberta — where it gets cold, really cold — seems an unlikely place to investigate the food crop. The likelihood of seeing rice flourishing on the prairie soil is as sub-zero as the temperature in winter. Yet scientists at the University of Alberta have taken up another of the big challenges of rice research — boosting the uptake and use of natural nitrogen. If they can meet the challenge, the impact could be on a par with successful C_4 conversion.

When asked, "What are the most important jobs of nitrogen?", Good responds: "You name it. It's the key nutrient." Without nitrogen, plants such as rice will not grow and produce plump grains. The more efficiently plants take up nitrogen from the soil, the higher the crop yield.

There is already one proven solution to a lack of nitrogen in soil: fertilizer. But, write Good and his associate Perrin Beatty, although applying fertilizer "revolutionized crop yield and food production worldwide", the advance came at a "heavy economic and environmental cost"³. In terms of cost, over the past 5 years the worldwide price of commercial fertilizer has ranged from US\$0.60 to \$1.00 per kilogram. Given that 80-100 kilograms of fertilizer are typically used on each hectare of rice, that soon adds up. Worse, much of the added nitrogen escapes into the soil and waterways. Because plants take up an average of 30-50% of the total available nitrogen, the excess nitrates can cause environmental damage, including algal blooms on lakes and coastal waters and acidification of soil, which, in turn, makes some land unsuitable for crops. The

application of fertilizer also results in the release of nitrous oxide, a potent greenhouse gas.

Good's group started looking at nitrogen largely by accident. While investigating stresses from drought and shortfalls of oxygen, the team discovered that crop plants that over-produce alanine aminotransferase (AlaAT), an enzyme that catalyses the transformation of amino acids, have enhanced nitrogen uptake. The researchers showed⁴ that if they insert a barley AlaAT gene, and a promoter - a molecular on-off switch — into canola, the plants use nitrogen more efficiently than control plants. The team has expanded its canola work, inserting AlaAT into rice and other cereal crops. The group has licensed its technology to agritechnology firm Arcadia Biosciences in Davis, California. Field trials with the enhanced canola showed that it uses two-thirds less nitrogen fertilizer than the conventional variety to generate the same yield.

Arcadia is keeping further findings close to its corporate chest, but Good understands that field trials of rice — as well as barley and wheat — show mixed results. Some plots thrive with minimal fertilizer, whereas others do not. It is likely, Good says, that the plant works differently in different environments, and soil condition could be a key variable. He suspects that the inconsistent results are slowing progress in the field trials. He adds that a negative attitude

"We need another green revolution to meet demands for food."

towards genetic modification in some communities may also be a roadblock to commercialization (see page S55).

The timeline for nitrogen-efficient rice is longer than for C_4 . "I honestly don't think we'll see commercial rice crops for 20 to 30 years,"

Good says. But he is confident that researchers will at least discover the environmental circumstances that determine whether *AlaAT*-enhanced rice performs well. And he is certain that the research will reveal "quite cool" findings along the way, even if his team has to struggle constantly for funding. "That's why every bit of grant money we get goes towards researching NUE [nitrogen use efficiency] in cereal crops. It's too visionary and too high risk for conservative funding agencies."

In the United Kingdom, plant scientist Edward Cocking is wielding bacteria instead of genes in the quest to help rice plants thrive with less added fertilizer. The University of Nottingham's Centre for Crop Nitrogen Fixation, of which Cocking is director, is part of an international network that is exploring ways to encourage cereal crops, such as rice, to attract nitrogen-fixing bacteria to take up residence in cells of the plant, from roots to leaves.

The idea was initiated by Borlaug, who observed decades ago that legumes, unlike cereal crops, have evolved a symbiotic relationship with a soil bacterium called rhizobia that fixes nitrogen inside specialized root nodules.



Because rice lacks such nodules, using a bacterium to fix nitrogen seemed like a hopeless task. But in 1988, Brazilian agronomist and microbiologist Johanna Döbereiner discovered a different type of bacterium, *Gluconacetobacter diazotrophicus*, in sugar cane that fixes nitrogen from the air, no nodules required. Why not try it with rice and other cereals, thought Cocking. "This was my 'a-ha' moment," he recalls, although it took a while to put the pieces of the puzzle together.

Cocking set to work about ten years ago. The result is N-Fix, a method of putting *G. diazo-trophicus* into the cells of plant roots. Once there, the bacterium colonizes all the cells of the plant. "It's environmentally friendly and can be applied to all crops," says Cocking. His group has already proved the concept in the laboratory and greenhouse with maize, rice, wheat, oilseed rape and tomatoes. The team is currently testing different delivery systems, among them coating seeds with *G. diazotrophicus* and inoculating seedlings with the bacterium.

The University of Nottingham has licensed the N-Fix technology to Azotic Technologies based in Chorley, UK, a company committed to commercial-scale nitrogen fixation. Field trials conducted in 2013 on wheat and oilseed rape showed that *G. diazotrophicus* provided between one-quarter and one-half of the recommended amount of nitrogen-rich fertilizer treatments, meaning that additional fertilizer use can be dramatically reduced. Azotic has not yet tested N-Fix with rice, but Cocking says discussions are under way about possible trials in Asia, particularly China, and parts of Africa. "The aim is to bring N-Fix to the market for farmers in the next few years," says Cocking.

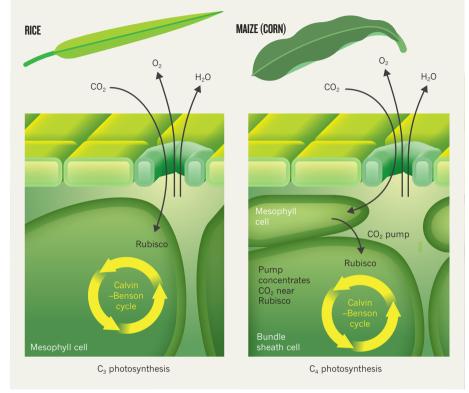
ANCIENT GENES, NEW ADVANCES

At the end of the wet season, wild rice flowers in lagoons, waterways and wetlands of Australia's Cape York peninsula at the far north of Queensland. "In many places it's growing in very large populations, occasionally as far as the eye can see," says Henry. The wild species flourishing in the very north of Australia are ancient. They are descendants of plants that lived 184 million years ago on the supercontinent Gondwana, which included the landmass of what is now Australia. It is even possible that Australia is the birthplace of rice, says Henry. Moreover, Australia's wild rice was neither domesticated nor interbred with domestic rice, as was Asian wild rice. That's why Henry and his teammates from the Queensland Alliance for Agriculture and Food Innovation put on their waders and risk encountering crocodiles to explore the wetlands. It is essential to collect samples from as many populations of wild rice as possible. "We're trying to do the genetics and understand reproductive biology, and identify species, pathology and the diseases and resistance that might exist," explains Henry.

The results gathered by Henry's team may help a team of international researchers

PHOTOSYNTHESIS VARIANTS

All green plants use the photosynthesis enzyme Rubisco to harvest carbon from carbon dioxide. C_4 plants have special 'bundle sheath' cells that concentrate carbon dioxide around the enzyme while blocking out oxygen, making the process more efficient.



studying blast disease. Many rice scientists consider blast, a fungal disease that affects crops in more than 80 countries to be the world's most important rice disease. The severity of a blast infection varies with year and location, and even within a field, depending on environmental conditions and crop management — yield losses can be as high as 50%.

But evidence is building that Australian wild rice plants have lived, apparently disease-free, with blast for thousands of years⁵. The wild rice is related closely enough to domesticated rice for cross-breeding without genetic tinkering. Clearly, the prospect of pinpointing blast-resistant genes and breeding them into domesticated rice is exciting. Plus, there is plenty of genetic diversity on offer that could improve other traits such as drought resistance. Henry's group has so far identified four species of Australian wild rice, including two newly discovered, unnamed species, suggesting even greater potential that is still untapped. These and other discoveries are being closely watched by the Oryza Map Alignment Project (OMAP), a rice research programme headed by geneticist Rod Wing at the Arizona Genomics Institute in Tucson. In July, OMAP researchers published the complete genome sequence of a hardy, stress-resistant African rice⁶. (For more on African rice, see page S64.)

The international team at OMAP has set itself the goal of unravelling the evolution, physiology and biochemistry of the genus *Oryza*, the group that includes domesticated Asian and African rice as well as Australian wild rice. "By understanding the entire genus at a genome level we have a whole new pool of genetic variation that can be used to combat pests and plant pathogens," Wing says. Decoding the genome is the easy part, he says. Understanding the code and applying discoveries to improve existing rice will take time.

Henry agrees that Australian rice has unique potential: as a laboratory for rice-breeding biology, as a source of disease-fighting genes, and even as a new commercial crop, but most of all as an important key to global food security. "The world has to recognize the value of this material," he says. Little wonder Henry and his colleagues are prepared to literally risk life and limb. As he says: "Don't worry about the crocs. This is the latest thing in rice."

Leigh Dayton *is a freelance science writer in Sydney, Australia.*

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Mothers and children in the Philippines protest in 2013 against golden rice, which is genetically designed to contain the vitamin A precursor β-carotene.

BIOTECHNOLOGY Against the grain

Golden rice could help to end a nutritional crisis – but only if researchers can overcome some daunting technical and political hurdles.

BY MICHAEL EISENSTEIN

The years of frustration are audible in Adrian Dubock's voice when he talks about the development of golden rice. "It's been an uphill struggle," he says, "but I think we're winning."

Golden rice was created in response to a nutritional crisis that grips some of the poorest communities in the world. According to the World Health Organization, every year between 250,000 and 500,000 children lose their eyesight because of vitamin A deficiency. Half of them will die within a year of going blind, primarily because their immune systems did not have enough vitamin A to function properly (see 'Prevalence of vitamin A deficiency').

Because golden rice is genetically designed to produce β -carotene — a precursor to vitamin A - it would seem to be an ideal solution to vitamin A deficiency in rice-dependent regions of the world. In many of these areas, including south and southeast Asian nations

such as India, Bangladesh, Indonesia and the Philippines, rice is the primary food source, comprising up to 70% of the daily caloric intake. "In the Philippines, they literally don't call a meal a meal if it doesn't have rice in it," says Dubock, who is manager of the Golden Rice Project.

Rice is relatively affordable and filling, but it has its shortcomings as a staple. For example, it is only a marginal source of many important vitamins and nutrients, including vitamin A. What's more, most grains undergo a polishing process that helps to prevent spoilage, but which also reduces the nutritional value even further, leaving consumers of rice-based diets vulnerable to malnutrition.

However, genetically modified (GM) agriculture remains deeply controversial, and scientific

and regulatory setbacks have stopped golden rice from reaching those who need it most. Dubock says that those who want to bring it to the masses

ONATURE.COM India's legal battle over growing GM crops reported here: go.nature.com/7g7bt9 must be ready to wage a multipronged campaign to overcome the research hurdles, win public confidence and inspire government support. It is bound to be a long road. But with so much at stake, Dubock is committed to moving forward, and he is not alone.

A PROMISING START

The seeds of golden rice were sown in 2000, when plant scientist Ingo Potrykus of the Swiss Federal Institute of Technology in Zurich and cell biologist Peter Beyer of the University of Freiberg in Germany first attempted to insert genes that control β -carotene synthesis into rice plants¹. The newly acquired β -carotene gave the rice a distinctive yellow-orange hue that led to its now familiar nickname, but it was unable to address the nutritional needs of vitamin A-deficient consumers. A collaboration with Swiss biotechnology company Syngenta, based in Basel, led to a greatly improved version that could deliver more than half of the recommended daily intake of β-carotene in a single serving. Syngenta

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subsequently transferred control of the product to the Golden Rice Project under the auspices of a humanitarian board of scientists and publichealth experts that, under the leadership of Potrykus and Dubock, has been tasked with making golden rice available to low-income farmers and researchers in the public sector throughout the developing world.

Potrykus and Beyer carried out laborious, trial-and-error testing of different combinations of metabolic genes and methods of introducing them into the rice genome. The initial version of golden rice, created with genes extracted from daffodils (Narcissus pseudonarcissus) and bacteria, produced only 1.6 micrograms of β-carotene per gram of rice, which was woefully inadequate for use as a dietary supplement. The improved version developed at Syngenta in 2005 replaced the daffodil gene with an equivalent gene from maize $(corn)^2$. Golden rice 2, as it became known, delivered far superior β-carotene production — up to 37 micrograms per gram — and safe delivery of β -carotene to human consumers has now been demonstrated in multiple trials.

REALITY BITES

Several technical problems have dogged golden rice's journey from the greenhouse to the field, however. Since 2010, the Philippines-based International Rice Research Institute (IRRI) and the Golden Rice Project have been working with the Philippine Rice Research Institute (PhilRice) to conduct field trials spanning three growing seasons at five sites across the Philippines.

Unfortunately, the golden rice strain selected for field testing does not grow as well as local rice varieties, limiting its appeal to struggling farmers. "The final product has to be so good that it will be readily adopted by farmers in terms of agronomic traits - yield, disease resistance, quality and ability to withstand adverse conditions — as well as β -carotene production," says Antonio Alfonso of PhilRice, who led the trials.

Identifying a gene combination that delivers enough β -carotene is only half the battle. Scientists must insert these genes into the genome of the rice plant in a way that allows them to be expressed without interfering with other genes. As a further complication, crops that work well in the lab may not be the same varieties that people like to eat and grow, so agronomists must perform a lengthy process of 'introgression' in which they breed the GM strain repeatedly with popular strains. The final goal is to produce plants that contain the new trait, but otherwise resemble local strains as much as possible.

Inadequate introgression may have prevented golden rice from thriving, says Inez Slamet-Loedin, who works on transgenic biofortified rice at IRRI. "Syngenta was working with an American rice variety that is not suitable for the tropics," she explains. Researchers at IRRI crossed this rice with tropical strains grown in the Philippines, but she estimates that the hybrids acquired only 82% of the local rice's genetic background. "We probably need that to



Golden rice (left) and conventional rice.

be closer to 98%," she says.

The position of the introduced genes may also have been problematic. Syngenta provided IRRI with six different 'insertion events' - individual rice strains with the β -carotene-producing maize genes incorporated at different sites in the genome. The golden rice research team focused on one particular insertion event known as GR2-R, which performed well in greenhouse testing but failed to thrive in the field. Subsequent investigation has suggested that the insertion site could be interfering with the expression of a gene linked to root development.

The golden rice team has access to multiple strains with distinct insertion events, but it focused on GR2-R to streamline the regulatory process surrounding testing. This is partly due to a document called the Cartagena Protocol on Biosafety, which has been ratified by 165

countries and the European Union. The protocol encourages special caution for the regulation of 'living modified organisms', defined as organisms "that possess a novel combination of genetic material obtained through the use of modern biotechnology". Given the expense and paperwork required to test any particular GM strain, most groups focus on a single event to lead through the regulatory process - essentially betting the house on a single spin of the wheel. "It would be much easier if you could just plant everything in the field and test it," says Matin Qaim, an economist at the University of Göttingen in Germany.

The IRRI researchers are shifting their focus to another event selected from the Syngenta pool, GR2-E. "This was our back-up all along so it's not like we're starting from zero," says Slamet-Loedin. "But we will need to generate some additional regulatory data." This is not as simple as it sounds, and Qaim says the switch has "cost a year or two in terms of further development".

THE GM STIGMA

The scientific problems can be solved, but public fears over GM organisms (GMOs) may be a bigger obstacle. Activists in Europe and North America have shaped the debate by raising doubts and concerns over the environmental impact and health risks of 'unnatural' GMOs, even though scientists have pointed to numerous studies that should assuage these worries. Dubock describes surveys in the Philippines that found that many farmers were interested in golden rice, even when educated about how it was created — until they heard the term GMO. Slamet-Loedin reports similar experiences

IRON RICE Rice can be used to deliver another key nutrient

Many communities that are short of vitamin A also lack other essential nutrients, such as iron. Scientists see an opportunity to use modified rice as a vehicle for this mineral, too. "Rice has the lowest iron level of any of the major cereals," says food biotechnologist Alexander Johnson⁵ of the University of Melbourne in Australia. Polished rice contains 2-4 parts per million (p.p.m.) of iron, he says, and it takes about 14 p.p.m. to improve the iron status of people who get most of their calories from rice.

Attempts to obtain iron-fortified rice by conventional breeding have yielded only a twofold improvement in iron content. But two genetically engineered strains - one developed by Johnson and his colleagues, the other by Wilhelm Gruissem's group⁶ at the Swiss Federal Institute of Technology in Zurich — could offer an alternative. Both use genes encoding nicotianamine synthase, an enzyme that increases iron transport within

the plant, and ferritin, a storage protein that helps draw iron from the environment.

Johnson's group is more than halfway through a five-year field trial in the Philippines and Colombia, and the early data are promising. "Under field conditions, we are obtaining rice with iron at 15 p.p.m. with no yield penalty and good grain quality," says Inez Slamet-Loedin of the International Rice Research Institute in the Philippines, whose team is collaborating closely with Johnson. Gruissem is seeking potential partners to move his rice from the greenhouse to field trials, but he has an even more ambitious goal — to engineer a single, super-nutritious crop with multiple biofortification traits. "We want to stack β -carotene production with iron or vitamin B6 production," he says. "We have the technology and we should try it out — although I would say it's going to be something of a 'regulatory adventure'." M.E.

working with nutritionists. "I met one who was so happy when he heard how it would make children healthier, but when I said it was a GMO he suddenly changed his mind," she says. "People have this image of it as a monster."

Greenpeace International, a respected nongovernmental organization with a long history of standing up for environmental causes, is one of the most prominent opponents of golden rice. As part of a broader campaign against GMOs, the group says that the rice may be unsafe to eat, might be harmful to the environment and could disempower local farmers. As an alternative, the group wants to see 'traditional' agricultural methods and conventional strategies of dietary supplementation.

In this climate, any minor misstep by golden rice scientists can become a major setback. For example, a study conducted in China in 2008 by nutrition scientist Guangwen Tang of Tufts University in Boston, Massachusetts, showed that a serving of golden rice was both safe and effective at boosting serum vitamin A levels in young

children³. Shortly after the study's publication in 2012, Greenpeace issued a press release claiming that the investigators failed to disclose that they were testing a GM strain, describ-

"It is not a 'magic bullet', but it is a potential instrument against malnutrition."

ing the push for golden rice as "irresponsible and dangerous" and condemning Tang's team for using "children as guinea pigs".

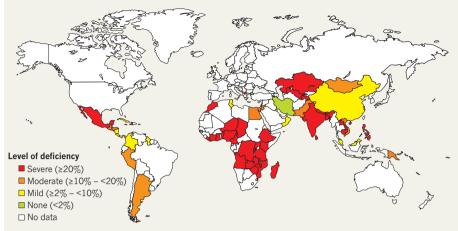
The Chinese government subsequently sacked three local scientists for their involvement. A review by Tufts concluded that the researchers had handled consent improperly by failing to adequately inform parents that the rice being tested was GM and inappropriately altering the study protocol after receiving institutional approval. Tang is now engaged in a legal battle with both the university and the American Society for Nutrition to fight the retraction of her study.

Greenpeace scientist Janet Cotter thinks it is too early to make assertions about the safety of golden rice. "You may very well be able to create β -carotene in rice, but then the question is, what else has changed?" she says. "There's no way you can test every single compound in a plant, and you still won't know about the food safety in terms of the wider population." But proponents of golden rice see this as an unnecessary objection to a promising solution to malnutrition. "We cannot ever say the risk from GM crops is zero," says Ronald Herring, a political scientist specializing in biotechnology policy at Cornell University in New York. "But I don't know of any actually authenticated hazard, and I think the science all points in the same direction."

The vigour of the opposition may seem surprising, given that golden rice was created to keep impoverished children healthy. According

PREVALENCE OF VITAMIN A DEFICIENCY

Map showing level of serum retinol (an indicator of vitamin A deficiency) in pre-school age children. Data were collected by the World Health Organization between 1995 and 2005 from populations at risk.



Estimates of vitamin A deficiency are based on low serum retinol concentration <0.70 µmol I⁻¹

to Qaim, this is precisely the problem: many in the anti-GM movement perceive golden rice as a Trojan horse that, if made widely available, will fundamentally alter the discourse about agricultural biotechnology. "They're looking for propaganda to show that we need GM crops," says Cotter.

Golden rice does sidestep many of the arguments typically marshalled against GM crops. A common environmental concern is that genetically engineered traits will disperse into other plant species, potentially resulting in undesirable consequences such as hardier weeds. But β -carotene is only beneficial for human consumers and offers no clear advantage for the plant itself. "It's not going to make those plants fitter," says Qaim. "It's not going to spread far."

Furthermore, the trait is being introduced into the rice strains normally grown by local farmers, so adopting golden rice will not leave growers beholden to biotech firms to purchase new seeds each season, nor should it alter their agricultural practices. Many opponents of golden rice argue that greater dietary diversity would be a better solution, and this is certainly true. Unfortunately, many of Asia's poorest and most malnourished people lack — and are unlikely to acquire — reliable access to mangoes, carrots or other fruits and vegetables rich in vitamin A. Golden rice, in contrast, could easily be integrated into local diets.

Unfortunately, each year of delay translates directly to lives lost through malnutrition. Qaim and his colleagues have analysed the potential health and economic benefits of adopting golden rice and estimate that the crop could potentially save up to 40,000 lives per year worldwide in a highly cost-effective manner⁴. The results from the human consumption trials in China suggest that, in some conditions, the return on the investment could be even greater. "Even our optimistic assumptions may be on the pessimistic side," says Qaim. "Not every consumer will grow or eat it, and this is not a 'magic bullet', but it is another potential instrument in the fight against malnutrition." The early results with golden rice have been so encouraging that other research groups are now investigating the use of rice as a vehicle to combat deficiencies of other essential nutrients, such as iron (see 'Iron rice').

GOLDEN FUTURE

The setbacks have been unfortunate, but the golden rice researchers are confident they will find a winning combination in the years ahead. The regulatory environment will be a decisive factor, and both Alfonso and Slamet-Loedin praise the support their project has received from the Philippine government. They are hopeful that their country will back commercialization once the safety and efficacy data roll in from the field trials. If the crop is good, they say, the benefits should sell themselves.

The governments and protestors are important, of course, but the tipping point for GM rice may come from the farmers themselves. As farmers start to recognize the advantages of some of these new rice strains, the seeds are bound to find their ways to paddies around the world, with or without official government sanction. Herring predicts that golden rice and GM foods in general — will someday revolutionize agriculture in much the same way that MP3 players changed the music industry.

One way or another, good ideas — and good crops — will eventually take root. ■

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Chinese farmers planting rice - humans domesticated grass many centuries ago but archaeologists are still investigating the crop's origin.

DOMESTICATION

The birth of rice

From a wild Asian grass to a refined crop that is the staple diet of half the world's population, the domestication of Oryza sativa spans centuries, but the grain's ancestry is hotly contested.

BY EWEN CALLAWAY

A sian civilization was built on rice on *Oryza sativa*, to be exact. The crop, which today is the primary food source for half of the world's population, transformed nomadic hunter-gatherers into stay-at-home farmers, spawned the first urban centres and built empires and dynasties. "Probably more so than any crop, it drove societies and economies to become densely populated, potentially more urbanized, and it also transformed landscapes," says Dorian Fuller, an archaeobotanist at University College London.

Despite — or possibly because of — rice's primacy, the history of the grain remains controversial, with little agreement on where, when and how many times humans tamed *O. sativa* in Asia to create the world's most important crop. (The only other domesticated rice species, *Oryza* glaberrima, has its roots in Africa. See 'The second story'.) "Almost every part of Asia had been pinpointed as the area where rice originated," says Michael Purugganan, an evolutionary geneticist at New York University who studies rice domestication. Unravelling the history of rice in Asia would illuminate a turning point in human civilization and give scientists fresh insight that could help improve the crop for the future. Thanks to advances in genetics and to new archaeological finds, that history is becoming clearer — and it is a lot more complicated and convoluted than anyone thought.

COMPETING CLAIMS

Oryza rufipogon, the Asian wild grass that is most closely related to *O. sativa*, is a sinewy, weedy plant. Its red grains are edible, but some modern rice growers consider it a pest. As humans started intentionally planting rice around 8,000 to 9,000 years ago, they sought out plants with the most desirable traits. Over time, the cultivated grass became stouter and straighter, producing heftier grains in greater quantities and that clung to the plant instead of tumbling to the soil — or 'shattering' — to facilitate spread. Claiming the title of the birthplace of rice would be a matter

of great pride for a nation. This, along with the wide geographical range of *O. rufipogon*, has led

> NATURE.COM To read more on the origins of cultivated rice, see: go.nature.com/t7qwzf to competing claims for domestication — including the Ganges valley in northern India, several locations in China, southeast Asia, the southern slope of the Himalayas and numerous other places. "Because rice is embedded within cultural identities within different nations in Asia, everybody wants to have had rice first," says Fuller.

For the past few decades, much of the focus on rice domestication has centred on China and India. In the 1960s and 1970s an influential Taiwanese agriculture scientist, the late Te-Tzu Chang, collected and cultivated wild rice from across Asia and proposed a band of domestication that stretches from northern India to southern China. As Fuller explains, this work encouraged Indian archaeologists to continue maintaining that rice came out of India, and the Chinese to claim that it came out of South China.

Perhaps both camps are correct. Han dynasty records dating back more than 2,000 years distinguish between two varieties of rice, *Keng* and *Hsien*, now known as *japonica* (shortgrained) and *indica* (long-grained) respectively. Research¹ comparing dozens of wild and domestic strains has suggested that *japonica* and *indica* are more closely related to distinct wild

varieties than they are to each other, pointing to two separate domestications: japonica in China and indica in India.

Indica and japonica clearly come from different genetic stock, says Tao Sang, a plant geneticist at the Institute of Botany of the Chinese Academy of Sciences in Beijing. But a closer look at those genes shows some surprising — and telling — overlap. In 2006, Sang's team identified a variation in a gene in domesticated rice known as sh4 that prevents rice grains from shattering². Japonica and indica share identical non-shatter mutations in sh4, suggesting that the two varieties had a shared history. Later studies suggested that the mutation arose in an ancestor of *japonica* rice first then found its way to indica. Since then, other teams have identified domestication genes that follow the same pattern: they appeared first in japonica before showing up in indica. One example is a mutation in a gene called Rc that lightened the seed coating, or pericarp³.

These discoveries sent rice scientists scrambling to explain how indica and japonica could be genetically distinct across most of their genomes yet share mutations responsible for the key traits that made rice easier to cultivate. Although the specifics are still hotly contested, most researchers have concluded that humandirected hybridization played an important part in the very early history of domesticated rice.

One leading theory comes from a 2011 study⁴ by Puruggunan and his colleagues that modelled the relationship of dozens of wild and domestic rice varieties. The study suggested that the domestication of japonica, most probably in China, was the watershed event in the history of Asian rice. From there it seems that japonica spread to India, where farmers intentionally hybridized it with their local rice to produce indica. The exact nature of that local rice is still a mystery. It could have been an early domesticated variety, or it could have been wild.

Whether the creation of indica from japonica counts as a separate domestication event "is somewhat a semantic issue", says Jeffrey Ross-Ibarra, an evolutionary geneticist at the University of California, Davis. The take-home message remains: the earliest fields of *japonica* — again, most probably in China - provided the key materials for the rice revolution in Asia.

ORIGIN STORIES

Exactly where in China japonica was domesticated is another lively debate. The lower stretches of the Yangtze River valley in eastern China had long laid claim to early domestication, based on the discovery of roughly 8,000-year-old grains in archaeological sites there. And so a team led by Bin Han, a geneticist at the Shanghai Institute for Biological Sciences of the Chinese Academy of Sciences, raised eyebrows in 2012 when they proposed the Pearl River valley in deep southern China as the birthplace. Han's team had compared the genomes of more than 1,000 domesticated

THE SECOND STORY The roots of African rice

A few thousand years after Asian farmers fully domesticated rice, ancient African farmers created a species of their own. African rice (Oryza glaberrima) generally does not produce as many grains as Asian rice, and although the crop never became a dominant staple, it was historically an important addition to some local diets (see page S64). In July, a team co-lead by Rod Wing, a geneticist at the University of Arizona in Tucson, reported⁶ the genome sequence of African rice, along with an analysis of

strains of rice and another 446 wild varieties from across Asia. They found that both indica and japonica were most closely related to wild varieties growing in the Pearl River valley. There is no archaeological evidence supporting early rice cultivation in the region, which is one reason why the claim remains controversial. But Han says that this could be because of the comparative poverty of its ancient inhabitants, who did not keep large stores of rice, unlike the richer Yangtze valley dwellers.

Archaeological work remains focused on the Yangtze. Since 2004, Fuller has excavated at a site in the lower Yangtze River valley that has been touted as an early centre of rice domestication. "I had always been taught, and all the textbooks will tell you, that there's early rice domestication here in 5000 BC," he says. But the history, he says, turns out to be a bit more nuanced. "My impression of visiting this site is that it's full of storage pits that are full of acorns. Nobody mentions the acorns."

In Fuller's view, the early inhabitants of this and other Yangtze valley sites were hunter-gatherers who dabbled in rice cultivation but mostly ate acorns, water chestnuts and fish. In a 2009 paper⁵ that analysed thousands of

microscopic rice remains from the site, Fuller's team documented a slight increase in the presence of domestic-looking rice, beginning around 5000 BC. But these rice grains kept changing shape - a sign of a crop not yet fully domesticated. Not until the shape stabilized thousands of years later did acorns disappear from Chinese archaeological sites. Rice domestication, as Fuller sees it, was a slow, haphazard enterprise.

In the hope of untangling rice domestication further, researchers are turning to the same ancient-DNA technologies that have revolutionized the understanding of human evolution. If they can recover DNA from ancient rice 20 domestic strains and 94 varieties of Oryza barthii, its closest wild relative. Their analysis suggested that the African rice was domesticated just once, probably near the Niger River in West Africa. What is more, they discovered that African rice has mutations near the same genes that control shattering in Asian rice, as well as other domestication traits. Although humans in Africa and Asia domesticated rice independently and thousands of years apart, they altered the crop's genome in similar ways, Wing says, E.C.

remains, researchers may be able to determine when and where the key domestication genes emerged. Most rice from archaeological sites is charred, and past efforts to glean DNA from grains have failed. But modern sequencing machines that can decode very short strands of DNA - likely to be the only ones left in rice that is thousands of years old - mean it may be possible to get DNA and even whole genomes from ancient rice. "The techniques are here, and the revolution is going to happen," says Fuller, who has begun a project with a team at the University of Warwick, UK, to sequence ancient rice DNA from China, India and Thailand.

Humans continue to shape the rice genome, but some researchers worry that intensive breeding for high yield and pest resistance has narrowed the genetic diversity of cultivated rice, leaving crops more susceptible to disease and less adaptable to the effects of climate change. Sang and other scientists studying rice domestication argue that contemporary rice breeders should take advantage of the handiwork of the humans who transformed wild grasses into the world's most successful crop. Ancient rice varieties no longer under widespread cultivation could

A pot from the Han dynasty, about 162 BC, for steamed food.

> high-yielding strains to feed a world of nine billion people, Sang says. "There's great potential in those ancient cultivars."

provide attributes to help

Ewen Callaway is a senior reporter at Nature.

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The team at the International Rice Research Institute who submitted data to the 3,000 Rice Genomes Project.

The search for the rice of the future

Scientists are hoping to make the world's most successful crop even better.

BY FELIX CHEUNG

wo farmers in different parts of the world can plant the same species of rice, but their crops may look strikingly different. Rice has enormous genetic diversity, and scientists are now developing the ability to take advantage of it. In May 2014, a group of researchers from the Chinese Academy of Agricultural Sciences (CAAS); the research organization BGI, based in Shenzhen, China; and the International Rice Research Institute in the Philippines published the genome sequences of 3,000 strains of rice collected from 89 countries1.

This endeavour, called the 3,000 Rice Genomes Project, allows scientists to identify the specific genes that control the traits that are most important for rice production. Their discoveries will undoubtedly lead to important insights into the history of rice domestication (see page S58) and, more importantly, will provide clear targets to further improve one of the world's most important crops.

Improvements are desperately needed. Advances in breeding and agriculture have greatly increased yields over the past few decades, but scientists warn that if current population trends continue, there won't be enough rice to meet demand by 2050 (see page S50). In addition, greater urbanization, water shortages, soil erosion and extreme weather resulting from climate change may threaten rice production and offset many hard-won victories. Rice researchers know they will have to

push the genetics even further if they are to keep pace and ensure rice's place as a staple food in the future. They also know that alongside

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For more on the genetics of Asian rice: go.nature.com/9pruwi the molecular genetics and biotechnological advances, there is still a place for the careful interbreeding of both domesticated and wild rice strains.

OLD-SCHOOL ADVANCES

Farmers have been using hybridization in one form or another for thousands of years, but the approach is still at the forefront of advances in rice production. In September 2013, researchers around the world applauded Yuan Longping — known as the father of modern hybrid rice — and his team at the China National Hybrid Rice Research and Development Center in Changsha when they unveiled their latest 'super rice' hybrid. The new strain, called Y Liangyou 900, yielded 14.8 tonnes per hectare — a record and more than double the average yield for rice in China². In field tests the rice produced 6.6% more grains than the previous record-holder, also developed by Yuan's team. The new strain puts China, the world's largest rice producer, firmly on track towards its target of achieving 15 tonnes per hectare in demonstration sites by 2015 and nationwide by 2020.

Y Liangyou 900 is the culmination of 40 years of careful crossbreeding and has every trait that would be expected from a super-productive strain of rice. It has strong roots, large panicles (secondary branches), a high seeding rate and large grains, and is resistant to stresses such as drought and insect infestations. And, as Yuan notes with pride, all this has been accomplished using old-fashioned interbreeding.

Over the decades, Yuan has shown many times that a deft touch with breeding can yield great rewards. In 1973 he developed his first hybrid rice, an *indica* (long grain) hybrid of three different strains that produced 20–30% more grains than conventional varieties. Every year since then has seen an increase in the average grain yield in China. Today, modern hybrids grow in 57% of rice paddies in the country and account for 65% of the national rice output³.

Many hybrid rice varieties are hardier and grow better than either of their parent strains, but it has not been entirely clear why. This phenomenon, known as 'hybrid vigour' or heterosis, is often seen in agriculture but seems to be especially strong in rice. An analysis⁴ published in 2009 found that genes related to energy metabolism and transport are especially active in hybrid rice *LYP9*, suggesting that these genes may be particularly important in the development of hybrid vigour.

GENETIC REVOLUTION

Despite all this progress, scientists acknowledge that hybridization alone won't provide enough rice to meet future demand. They will need to identify the genes that control particular beneficial traits and use the tools of biotechnology to improve the plant. The publication of 3,000 rice genome sequences is sure to help, but even before all this information became available, scientists had already found some genes that have proven to be game changers.

As recently as the early 1960s, most rice crops were tall varieties that were prone to tipping over under the weight of large, heavy grains. The solution was the development of a shorter, sturdier variety of rice called IR8 that could deliver the same amount of grain but was less prone to tipping. Widespread use of this new variety helped to drive Asia's 'green revolution' in the 1960s.

In 2002, a team led by geneticist Makoto Matsuoka at Nagoya University in Japan discovered⁵ that IR8 owed its short stature to a loss-of-function mutation of the semi-dwarf gene *sd1*. The group found that the genetic impairment led to defects in the biosynthesis and signalling pathways of gibberellin, the plant hormone responsible for controlling cell elongation. The cells were shorter, but in all other respects functioned normally.



Research into rice genetics is looking to minor genes to make small, accumulative improvements to yield.

Scientists are also targeting the genetic basis for other crucial aspects of rice production. "There are three key elements in grain yield: panicle size, grain number and grain size," says Jiayang Li, CAAS project director and a driving force behind the 3,000 Rice Genomes Project. "A rice plant in which these components are great would naturally have high yield."

In 2003, Li and his team identified a gene called *MONOCULM 1* (*MOC1*) that functions as the master control for shoot development⁶. They showed that rice plants that overexpress *MOC1* produce more auxiliary stems that branch out from the mother stem than normal, whereas those with a loss-of-function mutation in *MOC1* produce only a single, stout stem. Li now aims to find the right expression level for *MOC1* to decrease the number of stems while increasing the number of seed-bearing branches, which could lead to even more impressive yields. "Then the grains can become larger and heavier, thus the grain yield further improves," he says.

In theory, scientists could use genetic engineering to ensure that all rice breeds carry the most useful, high-yielding mutations. But it is not that simple. One potential obstacle is the widespread public opposition to genetically modified crops, but there are also many technological challenges to overcome. The MOC1 gene is a case in point: the loss-offunction mutation not only impairs the proliferation of stems, it also increases plant height and reduces the number of panicles. These unintended consequences are a reminder that grain yield is a complex agronomic trait controlled by not one but many regions of DNA. Moreover, most of the genes known to have a beneficial effect on yield have already found their way into common strains, limiting their ability to increase rice yield further.

If scientists are to revolutionize rice production, they may have to search for wild varieties that have rare gene variations. There is a precedent for this approach. In 1996, geneticists Pamela Ronald at the University of California, Davis, and David Mackill at IRRI set out to find a wild variety of rice that was particularly tolerant of flooding. A decade later they identified⁷ a cluster of three genes that is responsible for submergence tolerance, the ability to survive after being under water for two weeks. Ronald used precision breeding to introduce the key gene from the cluster into a strain from Bangladesh, where rice is particularly prone to flooding. Early trials showed that the flood-resistant gene improved yield by up to sixfold in some areas. The modified plant is now widely grown in other flood-prone countries, including India and Indonesia.

MINOR GENES AND MAJOR BENEFITS

Most investigations into the genetics of rice production have focused on genes that have a great effect on productivity. But such big-ticket genes don't tell the whole story. "Although each of these genes may improve yield by 3–5%, there are also hundreds of minor genes that can improve yield on a much smaller scale, say 0.5%," says geneticist Bin Han at the National Center for Gene Research of the Chinese Academy of Sciences in Shanghai.

Identifying these minor genes requires next-generation sequencing technologies and genome-wide association studies⁸. But once that is done, it raises the prospect of stacking minor genes together to improve the yield under a wide variety of conditions. "Within the next ten years, a breakthrough technology will emerge and we can begin using these minor genes in improving grain yield," Han says.

In Han's view, harnessing these minor genes is one more step towards a more productive future. Just as the plants of the early 1960s seem fragile and unproductive by today's standards, so the crops of coming decades may far outshine anything grown today. "I think we are on the edge of the next green revolution," he says.

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Rice is the main source of arsenic in food — it absorbs the metalloid more readily than other cereal grains.

CONTAMINATION

The toxic side of rice

Around the world, researchers are looking for ways to rid rice of a troublesome companion.

BY EMILY SOHN

alf the world's population eats rice every day, making the grain a major source of nutrition for billions of people. But there is often something nasty in those grains alongside the vitamins, minerals and carbohydrates. Because of the way rice is grown, it can harbour arsenic, which is a threat to human health¹.

"From all the work we've done over the years, it's quite plain that rice is the dominant source of inorganic arsenic in the human diet," says Andrew Meharg, a plant and soil scientist at Queen's University in Belfast, UK. "The cat's out of the bag. Now we have to do something about it."

The extent of the health risk is still unclear, but things are not looking good. Studies have linked chronic arsenic exposure with cancers of the bladder, lungs, skin and prostate, as well as heart disease. In the short term, it can cause gastrointestinal problems, muscle cramping and lesions on the hands and feet.

The risk of arsenic poisoning is greatest for people who eat rice several times a day, and for infants, whose first solid meals are often ricebased baby food.

In July 2014, the World Health Organization (WHO) set worldwide guidelines for what it considers to be safe levels of arsenic in rice, suggesting a maximum of 200 micrograms per kilogram for white rice and 400 µg kg⁻¹ for brown rice.

The situation is especially dire in Bangladesh, where rice is the national staple and the water is naturally high in arsenic. Here as many as 100 million people suffer from acute arsenic poisoning from multiple sources.

The problem of contaminated rice is not limited to Asia. A 2012 study by the US-based advocacy group Consumers Union also found worrying levels of arsenic in rice sold in the United States. Some samples contained arsenic at more than twice the safe limit recommended by the WHO. The group suggested eating no more than two or three servings of rice each week. But eating less rice is not an option in many parts of the world where the food is an irreplaceable part of the culture, diet and lifestyle (see page S50).

At first glance, the problem may seem intractable. Farmers do not have access to arsenic-free water, and people need to eat rice, even if it is contaminated. But scientists hope that innovations in genetics, microbiology, agriculture and even cooking can break the cycle and keep arsenic out of one of the world's most important crops.

MULTIPLE WHAMMY

A variety of metals can accumulate in rice, including cadmium, lead and mercury. But arsenic (strictly a metalloid, not a metal) is the biggest problem, partly because it naturally occurs worldwide in soil and water². It is especially common in the rocks of the Himalayas, from where the Ganges and other great rivers carry it to the heavily populated plains of south and southeast Asia. Most of the world's arsenic is locked up in mineral compounds underground, but mining and coal burning have released many tonnes into the environment (see 'Global arsenic cycle').

Rice is a particularly efficient scavenger of arsenic — it takes up ten times as much as other cereal grains - because it is the only grain traditionally grown in fields that are under water. Flooding makes soil conditions anaerobic, which causes arsenic to convert from bound and stable forms into more mobile ones.

In various states, arsenic has a similar chemical structure to phosphate and silicon, allowing it to sneak through the same pathways that plants use to absorb these important nutrients. Once inside, the arsenic becomes embedded in the roots, shoots, leaves and - particularly important for human health - the seeds. It accumulates most in the husk, the outer covering of the seed that is left intact in brown rice.

When rice is grown in an area with naturally high levels of arsenic, the problem becomes much worse. "It is a multiple whammy," says Shannon Pinson, a geneticist at the US Department of Agriculture's Dale Bumpers National Rice Research Center in Stuttgart, Arkansas. "It's in the soil and it's in the water that they're putting on the rice plants — and it's in the water they're cooking the rice in."

Some rice strains accumulate 20-fold less arsenic than others. This suggests that certain varieties may have developed a way of blocking its uptake, offering hope that breeding could give the same powers to other strains.

Pinson and her colleagues studied more than 1,700 strains of rice from around the world³. They found that some varieties from the United States contained significantly less arsenic than other rice varieties grown using the same soil and water. Even more revealing, when they crossed some of these low-arsenic strains with high-arsenic varieties, exactly one fourth of the second-generation plants had low arsenic accumulation. Following the logic of simple Mendelian genetics, this finding suggests that a

single gene is involved in the trait. However, the researchers have yet to figure out what gene it is, how it works, or even which of the plant's 12 chromosomes it can be found on. Other studies in Spain⁴ and the United States⁵ have flagged several genes and regions that may be involved in arsenic accumulation.

These and other findings raise the possibility of breeding arsenic resistance into strains from Bangladesh and other places where contamination is a major problem. Pinson says the idea of breeding low-arsenic rice is in its infancy, but "the best is yet to come".

GENETIC INTERFERENCE

Another way to prevent arsenic from accumulating in rice is to block its pathway from the roots to the grains. So far, researchers have discovered at least two types of transporter protein that carry the metalloid into the roots, says Barry Rosen, a molecular biologist at Florida International University's Herbert Wertheim College of Medicine in Miami. If scientists could identify the genes that govern the actions of these transporter proteins, they could potentially stop the flow of arsenic.

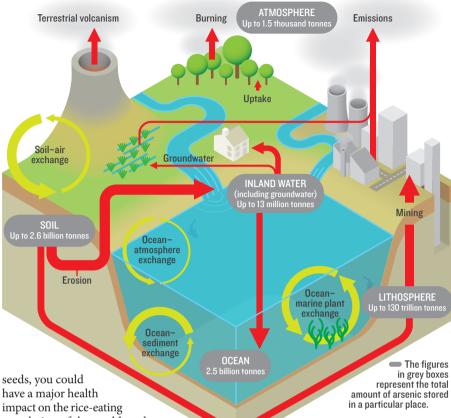
"We know some of the genetics, but I think there are many genes involved," says Yong-Guan Zhu, a biogeochemist at the Institute of Urban Environment at the Chinese Academy of Sciences in Beijing, who has collaborated with Rosen on several studies. "We are only exploring the tip of the iceberg."

Scientists hope that one day they can use genetic engineering to interfere with these arsenic-transport pathways, and there are many clever ideas for how that might work. Rosen and his group, for example, have created transgenic rice as well as transgenic soil microorganisms that both have the ability to turn arsenic into gas with the help of an extra enzyme originally discovered in algae that live in Yellowstone National Park⁶. Arsenic gas is not an ideal by-product, but Rosen says it would be quickly and safely diluted in the air. Some experimental rice strains have successfully released traces of arsenic in this way, but he says this is not yet efficient enough to be practical.

The prospect of genetic engineering opens the door for all sorts of big ideas. "If you could engineer rice to accumulate arsenic in the roots and not transfer it to the leaves and eventually the

GLOBAL ARSENIC CYCLE

Arsenic is a toxic element that is found in soil and water sources throughout the world. Arsenic can be found naturally in volcanic rock. Man-made sources include pesticides.



population of the world, and that is a huge population," says Julian Schroeder, a plant molecular biologist at the University of California, San Diego. "I think it's very doable. It just hasn't been proven yet."

A different idea is to target the microorganisms that live in the soil and help plants access nutrients. One low-cost approach would be to inoculate soils with microbes that make arsenic less accessible to plants, says Janine Sherrier, a plant biochemist at the University of Delaware in Newark. Sherrier and her team have already identified one candidate bacterium, referred to as UD1023, that deposits a layer of iron around the roots, slowing the uptake of arsenic. "There's no one golden solution," she says. "You have to use all the tools at your disposal."

The way rice is grown and processed offers other opportunities for intervention. It is possible to cultivate the grain in dry soils that are moistened only by rain. This method, known as upland rice cultivation, reduces the arsenic load by a factor of 30 compared with traditional flooded rice paddies, Pinson says. But this approach is not possible in many waterlogged low-lying areas, including much of Bangladesh.

Milling — removing the husk and turning brown rice into white - also removes much of the arsenic, which accumulates in the outermost layers of the grain. As a result, brown rice contains 10- to 20-fold more arsenic than white, but it also contains many beneficial nutrients such as fibre and niacin. Brown rice is popular in the

United States and Europe, but is still a novelty in Asia. Perhaps the easiest solutions of all lie in the kitchen. Instead of using equal parts water and rice when cooking, using three times more water than grain, and rinsing before and after cooking, can reduce the amount of arsenic by up to 30%.

Meharg says that he has developed a way of cooking rice that removes 80% of the arsenic contained in the rice grains. He cannot reveal details because the results have not yet been published, but he says the technique is simple and would require just a little low-cost engineering to create specialized cookers that would be affordable in even the poorest regions.

Anything that works is a welcome advance. "For the Chinese population, 60% of human arsenic exposure is from rice," Zhu says. "So if we can fix the rice problem, we can more or less fix arsenic exposure from food. It would make a huge difference."

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An African community winnowing its rice crop — this ancient farming practice separates the grain from the chaff and helps to remove pests.

The next frontier

Africa's newfound taste for an old grain has experienced problems — *drought, low yields and costly imports. But new projects are driving the continent towards self-sufficiency.*

BY KAREN RAVN

iets in Africa are changing. Traditionally, Africans have obtained their carbohydrate calories from maize (corn) and tubers such as cassava and sweet potatoes. But for the past three decades, rice consumption has been on the increase across the continent. "In the 1960s in Burundi, for example, rice was eaten only on feast days," says Joseph Bigirimana, regional coordinator for the International Rice Research Institute in east and southern Africa. "Nowadays, Burundians eat rice every day. And for some families, especially in cities, rice is eaten three times a day." A 2013 report by the International Grains Council, based in London, predicted that over the next five years rice imports would increase in sub-Saharan Africa more rapidly than in any other region in the world.

This newfound taste for rice is

understandable, says Gurdev Khush, an agronomist and geneticist at the University of California, Davis. Khush was behind some of the key breeding innovations that helped to ignite the green revolution, an agricultural awakening that brought new strains of rice and farming techniques to Asia in the 1960s. Khush notes that because rice takes much less time to prepare and cook than traditional African standbys such as cassava root, the grain is popular with people who have to cook dinner after a long day at work. Urbanization has also increased the demand for food that can be easily transported and stored. But production is not keeping up with rice's increasing popularity and the continent's growing population, so the gap between supply and demand keeps widening. To fill it, Africa imports a lot of rice, primarily from Asia (see page S50). At the last count, out of 21 million tonnes of rice consumed annually, only about two-thirds - 14.5 million tonnes - were home-grown.

Imports made up the 6.5-million-tonne shortfall, at a cost of US\$1.7 billion.

Closing this gap would have two major benefits for Africa: countries would spend less on rice imports, and the continent would be less vulnerable if the imports stopped or became prohibitively expensive. There is reason to worry about the price of rice. During the global food crisis of 2008, rice prices quadrupled within just a few months, from less than \$300 a tonne to more than \$1,200 a tonne on the world market. Some analysts predict that by 2020 an expanding population and shrinking resources will mean that Asia may no longer have any rice to export and may need to import it instead.

Africa is aiming for self-sufficiency in rice production, but that does not look imminent. "Africa imports a lot of rice and will continue to," says Chris Barrett, director of the Charles H. Dyson School of Applied Economics and Management at Cornell University in Ithaca, New York. "That's not going to change in the next five to ten years." What is changing is the way that rice is grown in Nigeria, South Africa, Kenya and other African countries. Scientists and farmers are teaming up to make the crop more sustainable, more productive and more important to Africa's future than ever before. AfricaRice, an independent consortium of 25 rice-producing countries in Africa, is optimistic about the challenge ahead. And, says its director-general Papa Abdoulave Seck, the "rice sector development can become an engine for economic growth across the continent".

RICE ECONOMICS

West Africa is the continent's leading riceproducing region, and the countries there are especially bullish about their ability to meet local demands. "Anybody who says Nigeria cannot be self-sufficient in rice production either does not know the country or does not know rice, or both, or is just being mischievous," says Martin Fregene, adviser to the country's agriculture minister, Akinwumi Adesina. If recent trends continue, Fregene predicts that Nigeria could produce enough rice to feed its people by 2016.

Countries such as Nigeria are taking aggressive economic approaches to encourage rice production — for example, by giving hefty tax breaks to anyone who grows and mills rice locally. In Nigeria, this arrangement has encouraged at least one of its citizens, multibillionaire Aliko Dangote, to ramp up his rice business. In August 2014, Forbes reported that Dangote had invested \$1 billion in rice production. He has purchased 150,000 hectares of farmland on which he plans to produce 1.4 million tonnes of rice every year, which he will then process in the largest rice mill in Africa — the one he intends to build.

In early 2014, the Bill & Melinda Gates Foundation in Seattle, Washington, and Germany's Federal Ministry for Economic Cooperation and Development made a different kind of investment in rice by founding the Competitive African Rice Initiative (CARI). This programme will benefit smallholder rice farmers who have a daily income of less than \$2 by helping them to produce rice that is more competitive in the local marketplace. Among other things, the programme is helping to identify the varieties of rice that are most sought after in the local markets and the facilities that will be required to grow and sell it. "We started with the market and worked our way backwards," says Richard Rogers, senior programme officer at the Gates Foundation.

BETTER YIELDS, BRIGHTER FUTURE

But encouraging people to grow and process rice is only part of the solution. A more direct approach to increasing rice production is to increase rice yield. And there is plenty of room for improvement in Africa, where the yield is very low, on average 2.2 tonnes per hectare



Nerica rice varieties are high yielding and hardy.

- much less than the world average, which is 3.4 tonnes per hectare, and only one-third of the average yield in China, the world's leading rice producer.

Regular and severe drought is one reason for Africa's low yield. Although rice does not have to be submerged in paddy fields to grow well, it does need a lot of water. Irrigation systems are expensive, so about 80% of farmers rely on rainfall alone. But in most places, there is not enough rain to ensure healthy crops. A study¹ spanning 1999 to 2003 found that yield for rice grown in rain-dependent lowlands was 2.0 tonnes per hectare, whereas in irrigated

lowlands the yield was 70% more.

Upland areas might

"Anybody who says Nigeria have more rain, but cannot be selfthey can lack nitrosufficient in gen. In some upland rice production areas, the yield is only does not know one tonne per hectare. the country, Fertilizers can supply does not know the needed nitrogen, rice, or is being but many farmers mischievous.³ do not have enough money to buy them —

at least in the quantities needed to significantly boost the yield.

In the absence of more money to build irrigation systems or buy fertilizers, the scientific solution is to breed new varieties of rice that need less water and less nitrogen. In fact, this is one of the most promising approaches to solving many of Africa's rice-growing problems.

Only two cultivated species of rice exist. Asian farmers domesticated one of them, Oryza sativa, and a few thousand years later African farmers domesticated the other, Oryza glaberrima (see page S58)². The two species have some traits in common but also significant differences. Crucially, O. sativa produces much higher yields, which gives it more obvious commercial value. It is the species that over the years has come to be grown all over the world. Ever since O. sativa was introduced into Africa, perhaps as early as the 1500s, O. glaberrima pretty much faded into the bush.

In the process, something was lost.

O. glaberrima is a survivor. It can thrive in harsh conditions that kill its Asian cousin³. In the 1990s, plant breeders at AfricaRice decided to try to get some of that hardiness back. They began crossing the two species, hoping to produce a new kind of rice that could be both high-yielding and tolerant. New Rice for Africa, or Nerica, was born.

Nerica is not a single variety of rice but rather a number of different varieties. In general, Nerica strains are high-vielding, producing nearly twice as much per hectare as traditional rice grown in the same conditions. Nerica plants also mature in a hurry, which gives weeds and drought less time to do their damage. Another big benefit is that they have a 25% higher protein content than the worldmarket average.

Specific Nerica varieties have been developed for various regional conditions. They may be resistant to devastating diseases that are endemic in some areas or to destructive pests that wreak havoc in others. And new varieties are being created all the time. In 2013, for example, the Alliance for a Green Revolution in Africa, a non-profit organization that promotes agriculture on the continent, partnered with the University of Port Harcourt in Nigeria to release three new lowland varieties that were long-grained, high quality and resistant to stresses such as iron toxicity and drought.

In 2005, seven West African countries received funding from the African Development Bank to finance the distribution of Nerica. Farmers chose varieties to grow on the basis of their needs. At the beginning of the project, Nerica strains were being grown on 200,000 hectares across all of sub-Saharan Africa. By 2011, they covered at least 800,000 hectares. Pre-project rice yield was about 1 tonne per hectare in the uplands, but yield now averages 2.5 to 3 times as much. Over the six years of the project, participating farmers earned \$14.4 million more than they would have done otherwise, and the roughly 35,000 members of their households rose above the poverty line of \$1.25 a day.

Many researchers see parallels between Africa today and Asia in the early 1960s. Asia was then on the brink of a green revolution that improved food security, revitalized economies and stabilized governments. Recreating the Asian green revolution in Africa would be a tall order. But with a combined effort by scientists, farmers, governments and investors, African rice could enter a new era, and history could be repeated.

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PERSPECTIVE



Time to unleash rice

Corporate inefficiency and government meddling are curbing production of the vital crop in the countries that need it most, says **Robert Zeigler**.

rowing rice should be a reasonable way to make a living. After all, half the people in the world depend on rice as their staple food. But even in an age of remarkable agricultural advances, millions of rice farmers and their families continue to scrape by at the very edge of existence. Scientists have made progress in understanding the rice plant. More than ever, they understand the genetics, growing conditions and agricultural techniques that can lead to improved yields. Further insights will open the door to future revolutions in rice productivity, even in the face of a changing climate and other challenges. But there is a risk that many farmers will be left behind.

The current system of rice production is rife with inefficiency, from the paddies to the village trading posts to the international market. Seed companies are doing too little to support the rice-growing industry. At the same time, governments of rice-producing countries are trying to do too much. For the sake of small-scale farmers — and world food security private enterprises and governments need to

unleash rice's potential to promote stability.

Seed companies have become central to the story of rice. Today, many companies are creating an array of hybrid strains that have been specially bred to withstand pests and produce more grains, but many farmers miss out on these innovations. Different strains thrive in different conditions — a variety that grows well in a high latitude may struggle in the hot, wet tropics. But some companies make little effort to match their hybrid offerings to local conditions, especially in the most impoverished areas. And although hybrids can produce impressive yields, they often have inferior grain quality, which makes the rice hard to sell at the market, a big problem for farmers whose livelihoods depend on sales. Worse, hybrid seeds can cost ten times more than inbred

rice as companies try to immediately recover the costs of research and development. Not surprisingly, many farmers choose to reuse the seeds from the same inbred varieties that have remained basically unchanged for hundreds of years, with the unfortunate consequence that they lose any chance to improve their harvests or their bottom line. They simply cannot grow the same rice in the same ways and hope for better harvests and bigger profits.

Thanks to advances in genetics, the strains available to seed companies are bound to improve. The May 2014 publication of the results of the first stage of the 3,000 Rice Genomes Project — a programme funded by the Bill & Melinda Gates Foundation and the Chinese Ministry of Science and Technology to sequence 3,000 rice strains — means that scientists will soon be able to identify many key genes that govern traits such as the quality of the rice grains and resistance to stress (The 3,000 Rice Genomes Project *GigaScience* **3**, 7; 2014). But it is time past time, really — for the seed companies to do their share. Instead of offering the same hybrids to every customer, no matter what the local needs or preferences are, imaginative companies must find a way to get superior seeds, including inbred varieties as well as hybrids, to rice farmers. Tailoring seeds to the needs of farmers will take research, time and a hefty initial investment, but the company that can successfully bring hardy, high-producing, affordable rice to the paddies of the tropics in India, Bangladesh, Vietnam and elsewhere will profit handsomely, and so will the farmers.

TRADE-OFF

Government policies that stifle the rice trade are an impediment to growth and prosperity. In most Asian countries, rice permeates the culture, and the suggestion of rice shortages can translate into a social crisis. To avoid this, governments often limit exports to prevent scarcity. This approach stands in contrast to wheat — a global staple that is traded internationally as a commodity, not as a cultural symbol or political tool.

If there is a rice policy that hinders the market and hurts either farmers or consumers, you can be sure that at least one country has tried it. Some, including Vietnam, intentionally keep rice prices low to make it

THE COMPANY THAT CAN BRING HIGH-PRODUCING, **AFFORDABLE** RICE TO THE PADDIES OF THE TROPICS WILL PROFIT **HANDSOMELY.**

more affordable for consumers, but this impoverishes farmers and discourages them from investing in hybrid rice or better equipment. Thailand recently took the opposite approach by paying farmers inflated prices for rice to boost their income. Although laudable in intent, the policy killed the country's once-lucrative rice export market. Thai rice became so expensive that international traders were reluctant to buy it. Reuters reported that by the end of May 2014, the country had lost US\$9.9 billion from a 16-month scheme to help rice farmers, leading to a financial crisis with repercussions that are still being felt. The then-prime minister, Yingluck Shinawatra, who had been elected in 2011 largely on the basis of her promises to help farmers, was deposed in a military coup in May.

Erratic government intervention in the interna-

tional rice trade causes far more problems than it solves. Sudden trade moratoriums imposed by India, Vietnam and some of the world's other major rice exporters during the global food panic of 2007 and 2008 increased the average price of internationally traded rice by more than 160%. Governments must first relax their rice policies so that surpluses can be traded openly on the international market. Rice farmers, even small-scale ones, can benefit from an orderly and transparent market. If farmers can have some confidence about what their crop will be worth, they can plan ahead and make better decisions at planting time. This will require the creation of a global, or at least regional, rice exchange where prices are negotiated and published daily.

It is up to the rice-growing countries of the world and the private sector to bring rice into the modern age. Growing the right varieties in the right places, under the right policies, and traded openly for the right prices will create stability — in the food supply, in financial systems and in governments — that is sorely lacking today.

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