Breeding ~5 to 10 years Present Elite cultivar

Genetic diversity for disease resistance in wheat has been lost through bottlenecks imposed by polyploidization, domestication, and breeding. Resistance genes from wild relatives of wheat, followed by their introduction by transformation into the elite crop varieties. There is, however, a barrier to such progress: Wheat, a worldwide staple food, has become an orphan among genetically modified (GM) crops.

GM crops—mainly corn, cotton and soybean—that contain transgenes for herbicide tolerance and insect resistance have significantly increased profit margins for farmers, by their introduction by transformation into the elite crop varieties. There is, however, a barrier to such progress: Wheat, a worldwide staple food, has become an orphan among genetically modified (GM) crops.

Wheat—the cereal abandoned by GM

Genetic modification of wheat for disease resistance could help stabilize food production

By Brande B. H. Wulff1 and Kanwarpal S. Dhugga2

The sudden appearance of crop diseases can cause an irreparable economic shock, particularly to smallholder farmers in developing countries. Wheat blast, for example, is a devastating fungal disease from South America, which emerged in Bangladesh in 2016 (1). It is currently controlled by quarantine but could easily spread to other wheat-growing areas, which could threaten food security. Furthermore, widespread crop failure from stem rust has occurred in Kenya and Ethiopia. Recent advances could provide a solution to this problem through the rapid discovery and isolation of disease-resistance genes from wild relatives of wheat, followed by their introduction by transformation into the elite crop varieties. There is, however, a barrier to such progress: Wheat, a worldwide staple food, has become an orphan among genetically modified (GM) crops.

GM crops—mainly corn, cotton and soybean—that contain transgenes for herbicide tolerance and insect resistance have significantly increased profit margins for farmers (2). Although GM rice is not yet commercially grown, several traits have been approved, for example, insect resistance, herbicide tolerance, and biofortification with provitamin A (3). The only application for the approval of a GM trait in wheat, herbicide tolerance, was abandoned in 2004 in the United States, and, apparently, no other trait has since been submitted for regulatory approval (3). Transgenic introduction of a gene that conferred resistance against Fusarium, a fungus that kills the grain-bearing organ in wheat and contaminates remaining grain with toxins, was ostensibly successful (4), but there is no record of an attempt to obtain approval for commercial planting of the GM crop. It appears that pressure from anti-GM consumer groups, mainly from Europe and Japan, on producers and unattractive profit margins for developers have relegated wheat to a low-priority crop. The agricultural seed industry charges a premium on GM seeds. Wheat is grown mostly on marginal land in the United States and generates only ~20% of farm income compared with maize, making it questionable whether industry can recover the costs associated with research investment. If and when GM wheat becomes available, countries in Africa and Asia, where food security is a perpetual concern, might be receptive to GM wheat, provided its use helps to stabilize production.

Wheat is grown on more land area than any other cereal crop, and it is second only to maize in grain production (see fig. S1). On average, wheat provides ~20% of the daily calories and protein per capita worldwide (5). With increasing global population and urbanization, demand for wheat is expected to increase, which will require an increase in the current rate of global yield gain of ~1% per year (5) (see fig. S2). Current potential grain yield, which is the amount of grain produced under nonlimiting inputs in the absence of abiotic or biotic stresses, is reportedly ~12 metric tons per hectare for wheat; however, the actual harvested yield is less than 4 metric tons per hectare (6). Suboptimal farm inputs, unpredictable environmental fluctuations, and diseases are some of the factors that suppress the yield potential. Genetic selection of stable varieties adapted to adverse climatic factors—for example, high temperature—is perhaps the most suitable avenue to mitigate the effects of unpredictable variables. However, changes in management practices and a readily available tool kit to guard against diseases are certain to help narrow the yield gap (7).

The ancestral hybridization events that gave rise to cultivated wheat, through polyploidization of the genome, followed by domestication and breeding, sampled only a fraction of the available genetic diversity, creating genetic bottlenecks at each stage (see the figure). This progressive narrowing of the genetic base resulted in a modern crop that is highly vulnerable to disease. The...
ability to incorporate disease resistance from breeding with exotic grass (wheat) species can compensate for this lack of genetic diversity. However, in practice, crossbreeding is a resource-intensive, time-consuming process because the generation time of wheat is 4 to 5 months. Speed breeding, which halves the generation time of wheat under artificial growth conditions (8), could allow a much faster incorporation of exotic resistance genes. However, limitations persist, including sexual incompatibility and linkage drag, the latter resulting from the co-introduction of linked, deleterious genes from the donor parent. Indeed, the potential of many exotic resistance genes is untapped owing to the burden of linkage drag. More importantly, when single resistance genes are deployed in a disease hot spot, they are often rapidly overcome by resistance-breaking strains of the pathogen, dissuading many breeders from undertaking this strategy.

As a result, the genetic treasure trove for disease resistance in wild relatives of wheat remains a largely underutilized resource in wheat breeding. If multiple disease-resistance genes from wild wheat relatives were cloned, these could be introduced as a multigene cassette by transformation into the wheat genome to provide broad-spectrum multilayered resistance that could delay the evolution of resistance-breaking pathogen strains (9). Such a cassette, or GM stack, would have the added benefit of being free from linkage drag. Moreover, unlike in the natural genetic makeup, in which the individual genes may be scattered throughout the genome, a cassette would ensure that the genes stay together in a breeding program, thus eliminating the risk of individual genes being separated from the stack and being overcome by the pathogen, causing piecemeal weakening of the stack and eventual breakdown.

Cloning disease-resistance genes from wild wheats, however, presents several challenges, including the complex, polygenic nature of durable disease resistance and seed and growth morphologies that are incompatible with existing mechanized cultivation. These issues conspire to limit the scope of traditional gene-cloning technologies, which require a disease-resistance gene to be genetically isolated in an otherwise susceptible background, followed by the generation and screening of large laboratory-produced populations (10). However, population genetics combined with next-generation sequencing is now reaching an inflection point at which it can deconvolute the complex relationship between genetic structure and phenotypes in a natural population to rapidly identify causal gene variants (11). Therefore, by selectively sequencing the repertoire of immune receptors (which detect molecules expressed by pathogens) and correlating these genotypes with disease susceptibility across a population of wild wheats, it seems possible to rapidly discover and identify (clone) the underlying disease-resistance genes (12) (see the figure). These and other technologies are likely to fuel an exponential growth of cloned disease-resistance genes. Moreover, cereal transformation technologies have improved to the point where inserting large stacks directly into elite cultivars should not provide a technical barrier (13).

Is wheat ready to come of GM age? A compelling case concerns wheat blast, a destructive disease in Brazil and other countries of South America. In 2016, it appeared in Bangladesh, causing widespread devastation (1). This disease now threatens to undermine food security in South and Southeast Asia, the world’s largest wheat belt, where 300 million undernourished people consume more than 100 million metric tons of wheat per year. Very little resistance to wheat blast has been reported in cultivated wheat (14). However, genetic variation for resistance can be found in the goosagrass *Aegilops tauschii*, a wild progenitor of wheat (15).

A wheat blast–resistance gene stack would have an excellent chance of halting the spread of the pathogen in Southeast Asia owing to the extreme genetic bottleneck in the pathogen imposed by its single incursion from South America. Because the pathogen was likely imported through contaminated grain, a key to success will be to ensure that there are no further incursions leading to increased genetic diversity in the pathogen population. However, because the pathogens causing wheat and rice blast are genetically similar and are both known to occur on other grass hosts (13), there is a risk that they could recombine and give rise to virulent forms that would infect both rice and wheat, creating a continuous disease cycle, or “green bridge,” in the rice-wheat rotation cropping system (whereby growing these two crops is rotated in the same year) that is practiced across much of Bangladesh, northern India, and southern China. Therefore, it is important that further proliferation of the pathogen in the region is curbed as soon as possible by the introduction of resistant wheat varieties.

Southeast Asia undoubtedly needs a solution to wheat blast, but if a GM solution existed, would it be adopted? Bangladesh seems likely to take the first step. The country comprises a burgeoning population, supported by intensive agriculture with up to three crops per season. Its framework for deregulating GM crops is rapidly maturing. It recently approved GM eggplant with insect resistance, is in the process of deregulating GM potato with late-blight resistance, and is close to releasing golden rice fortified with provitamin A. Bangladesh must import wheat to meet national demand, so there is no risk of upsetting a national export market with GM wheat, which is banned in many countries. However, if wheat blast were to spread into the Punjab in northern India, then it could prove challenging to control stewardship of a GM blast-resistant wheat line used in this region, potentially affecting India’s wheat export market.

Although the Bangladeshi Ministry of Agriculture supports GM crop cultivation, it may have to adopt other measures while the political and social stalemates on GM crops exist. However, to deliver yields to support the populations of the region and ensure continued protection of these yields, wheat must eventually become part of the GM family. ■

**REFERENCES AND NOTES**

3. www.isaaa.org/gmapprovaldatabase/

**ACKNOWLEDGMENTS**

The authors thank T. Islam, R. Singh, P. Nicholson, A. Galvin, and B. McDonald for helpful discussions. The B.B.H.W.I. lab is supported by the Biotechnology and Biological Sciences Research Council and the 2Blades Foundation. The K.S.D. lab is supported by the Consultative Group on International Agricultural Research (CGIAR) Research Program on Wheat (WHEAT).

**SUPPLEMENTARY MATERIALS**

www.sciencemag.org/content/361/6401/451/suppl/DC1

10.1126/science.aat5119
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Science 361 (6401), 451-452.
DOI: 10.1126/science.aat5119