*Annals of Botany* **100**: 999–1008, 2007
doi:10.1093/aob/mcm139, available online at www.aob.oxfordjournals.org

OXFORD JOURNALS
OXFORD UNIVERSITY PRESS

REVIEW

# The Importance of Barley Genetics and Domestication in a Global Perspective

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Received: 15 December 2006 Revision requested: 26 March 2007 Accepted: 22 May 2007 Published electronically: 30 August 2007

• *Background* Archaeological evidence has revealed that barley (*Hordeum vulgare*) is one of the oldest crops used by ancient farmers. Studies of the time and place of barley domestication may help in understanding ancient human civilization.
• *Scope* The studies of domesticated genes in crops have uncovered the mechanisms which converted wild and unpromising wild species to the most important food for humans. In addition to archaeological studies, molecular studies are finding new insights into the process of domestication. Throughout the process of barley domestication human selection on wild species resulted in plants with more harvestable seeds. One of the remarkable changes during barley domestications was the appearance of six-rowed barley. The gene associated with this trait results in three times more seed per spike compared with ancestral wild barley. This increase in number of seed resulted in a major dichotomy in the evolution of barley. The identification of the six-rowed spike gene provided a framework for understanding how this character was evolved. Some important barley domestication genes have been discovered and many are currently being investigated.
• *Conclusions* Identification of domestication genes in crops revealed that most of the drastic changes during domestication are the result of functional impairments in transcription factor genes, and creation of new functions is rare. Isolation of the six-rowed spike gene revealed that this trait was domesticated more than once in the domestication history of barley. Six-rowed barley is derived from two-rowed ancestral forms. Isolation of photoperiod-response genes in barley and rice revealed that different genes belonging to similar genetic networks partially control this trait.

**Key words:** Barley, *Hordeum*, domestication gene, genome evolution, common ancestor, *vrs1*.

## INTRODUCTION

Some 10 000 years before present (BP) ancient farmers selected wild species leading to domestication of crops on which humans are dependent today. During this agricultural revolution, people saved seeds from plants with favoured traits for the next generation, and over time they converted seemingly unpromising wild species into reliable and bountiful crops (Doebley, 2004). Modification included increase in the number of seeds, improved seed fertility, change in plant architecture, change in seed size and shape, adaptation of flowering time to different areas, and loss of seed shattering.

*Hordeum*, *Triticum* and *Secale* belong to the tribe Triticeae, the Poaceae family. Poaceae is considered to be monophyletic; therefore all grasses belonging to this family may have evolved from a single ancestor (Devos, 2005). The genus *Hordeum* consists of 32 species and 45 taxa including diploid ($2n = 2x = 14$), tetraploid ($2n = 4x = 28$) and hexaploid ($2n = 6x = 42$) cytotypes (Bothmer *et al.*, 1995). The majority of *Hordeum* species are perennials and different species have different reproductive systems (Bothmer *et al.*, 2003). Cultivated barley (*H. vulgare* ssp. *vulgare* L.) and its wild progenitor (*H. vulgare* ssp. *spontaneum* C. Koch.) belong to a single biological species, which is an annual and is diploid. No crossing barriers have been developed between the wild and cultivated forms, therefore spontaneous and artificial crosses are easily obtained (Asfaw and Bothmer, 1990). There has been a high frequency of introgression in areas where the wild and cultivated forms are in close contact.

The immediate ancestor of cultivated barley was first discovered in Turkey by the German botanist Carl Koch, and described by him as a separate species, *H. spontaneum*. However, based on the biological species concept (Bothmer *et al.*, 1995), the progenitor form is nowadays regarded as a subspecies [ssp. *spontaneum* (C. Koch) Thell.] within the same major species, *H. vulgare*, as cultivated barely (ssp. *vulgare*) (Bothmer *et al.*, 2003). The first definite sign of barley cultivation has been recorded from the Middle East 'arc' more than 10 000 BP (Zohary and Hopf, 2000). To investigate the time and place of barley domestication, the study of genes related to key steps in domestication can give valuable insights. In this review, recent progress in understanding the transition of wild barley to domesticated forms is described by focusing on genetics and biological functions of important traits that have been induced during the domestication of barley cultivars.

## IMPORTANT TRAITS FOR BARLEY DOMESTICATION AND MIGRATION

During the process of domestication, barley has gradually accumulated traits that facilitated agricultural production. Selection may have been unconscious, i.e. as a result of

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environmental selection or conscious as a result of deliberate choice by man (Bothmer *et al.*, 2003). Three key traits – selection for non-brittle rachis, six-rowed spike and naked caryopsis – were involved in barley domestication (Salamini *et al.*, 2002). These mutations are associated with the transition of wild barley to cultivated barley. Migration of barley to regions outside its place of origin was accelerated through mutations to develop reduced vernalization requirement and photoperiod insensitivity (Bothmer *et al.*, 2003). Barley was spread to different geographic areas by the accumulation of diversity for these traits.

### *Non-brittle rachis*

The most important trait for barley domestication is probably non-brittle rachis. Non-brittle rachis results in efficient harvest without loss of grains. Spikes of the non-brittle mutant remain longer on the plant in the field after maturation, so spikes with this mutant were harvested with higher frequency than spikes with brittle rachis by ancient farmers (Bothmer *et al.*, 1990). Seed dispersal systems are designed to enable wild plants to survive in nature, but the loss of natural dispersal mechanisms was essential for agriculture. The earliest archaeological clue for non-brittle barley comes from Tell Abu Hureyra from 9500 BP (Hillman *et al.*, 1989). Seed shattering in barley has two forms: brittle rachis and weak rachis (Kandemir *et al.*, 2000, and references cited therein).

In *Hordeum*, spikes disarticulate immediately above each rachis node to form typical wedge-shaped spikelets (Bothmer *et al.*, 1995). Disarticulation scars in wild barley are smooth which helps in seed dispersal, whereas in cultivated barley threshing produces rough dehiscence scars on grains detached from rachis segments. Anatomically, the rachis nodes are clearly constricted in brittle spikes, but are not constricted in non-brittle spikes (Ubisch, 1915). The brittleness of the rachis in barley promotes seed dispersal together with the rough awn, which can become attached to animals for effective dispersal (Bothmer *et al.*, 1995).

The most important non-brittle rachis genes for barley domestication are *btr1* and *btr2*. Takahashi and Yamamoto (1949) clarified the monogenic recessive inheritance of non-brittle rachis of cultivated barley based on crosses between cultivars and ssp. *spontaneum*. Two-way test crosses revealed that two independent recessive genes (*btr1* and *btr2*) cause non-brittle rachis (Takahashi and Hayashi, 1964). *Btr1Btr2* (double dominant genotypes) strongly constrict the rachis node, whereas one recessive allele *btr1Btr2* or *Btr1btr2* does not result in constriction of the rachis node (Ubisch, 1915). These recessive genes have been independently established by natural mutations from wild progenitors, which have a brittle rachis (Fig. 1; Takahashi, 1987). The two genes are tightly linked (Takahashi and Hayashi, 1964) and located on the short arm of barley chromosome 3HS (Fig. 2; Komatsuda and Mano, 2002). The recessive nature of non-brittle rachis suggests a mutation for loss of function in *Btr1* and *Btr2*. Phylogenetic studies using markers closely linked to *btr1*/*btr2* determined that cultivated barley consists of two geographic types, western and eastern (Komatsuda *et al.*, 2004; Azhaguvel and Komatsuda, 2007). These results support two independent domestication hypotheses of barley as proposed by Takahashi (1955).

Allelic variation was implied from *Btr1* and *Btr2*. Alleles of *Btr1.a* and *Btr2.k* complementary produced brittle rachis in the presence of the dominant D gene (chromosome 7H), whereas *Btr1.h* and *Btr2.h* of wild barley do not need the D factor to produce brittle rachis (Komatsuda and Mano, 2002; Senthil and Komatsuda, 2005). Komatsuda *et al.* (2004) showed two QTLs on chromosomes 5H and 7H (the D gene) for brittle rachis in addition to *Btr1* and *Btr2*.

Brittle-rachis genes are located on homeologous group 3 chromosomes in *Hordeum*, *Triticum*, *Aegilops*, *Dasypyrum* and *Thinopyrum* (Watanabe and Ikebata, 2000, and references cited therein; Li and Gill, 2006). It remains to be determined whether they are orthologous or not. Konishi *et al.* (2006) identified rice shattering gene *qSH1* which encodes a BEL1-type homeobox gene. The *qSH1* gene is located on the long arm of rice chromosome 1. Barley chromosome 3H and rice chromosome 1 are syntenous (Devos, 2005), and *JuBel2* (the barley orthologue of *qSH1*) (Li and Gill, 2006) was mapped on the long arm of barley chromosome 3H (Fig. 2; Müller *et al.*, 2001; Castiglioni *et al.*, 1998). As *JuBel2* and *btr1/btr2* are located in different arms of barley chromosome 3H, *JuBel2* does not correspond to barley *btr1/btr2*. Therefore, the *btr1* and *btr2* genes remain to be cloned. To elucidate the origin of cultivated barley, cloning of non-brittle rachis genes will be necessary. The *btr1* gene has been fine-mapped and is now delimited to a 0·84-cM region using AFLP-derived STS markers (Azhaguvel *et al.*, 2006).

### *Six-rowed spike*

During the process of cereal domestication, humans have selected in wild species toward the general direction of increased yield (Harlan *et al.*, 1973). One of the most conspicuous selections for increased seeds was the appearance of a six-rowed spike during barley domestication in the Middle East. Six-rowed barley produces three times as many seeds per spike as two-rowed barley and is a change of dramatic agronomic importance. Various theories have been proposed to the evolutionary pathway of six-rowed cultivars. Åberg (1938) assumed that six-rowed cultivated barley derived from a six-rowed form with a brittle rachis known as *H. agriocriton* found in the early 1930s in western China. Another theory assumed a single evolutionary line from ssp. *spontaneum* to ssp. *vulgare* (Fig. 1) which is nowadays in favour with barley scientists. Remains of six-rowed barley appear very early in the aceramic Neolithic beds in Tell Abu Hureyra from 8800 BP onwards (Helbaek, 1959; Zohary and Hopf, 2000). Archaeological evidence comes from Ali Kosh (Helbaek, 1969) where remains of two-rowed barley are dated at about 9000 BP with sporadic six-rowed elements among the two-rowed materials. This is a sign that the six-rowed character in barley was derived from two-rowed barley during domestication.

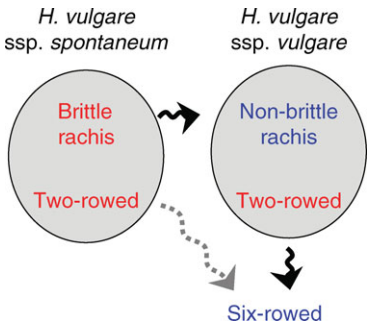


FIG. 1. A schematic diagram of the domestication process in barley regarding brittle rachis and row-type.

The spike architecture of *Hordeum* species is unique among the Triticeae, which possess three spikelets at each rachis node (Bothmer and Jacobsen, 1985; Bothmer *et al.*, 1995). Exhibition of the two-rowed phenotype in wild barley suggests that the two-rowed spike is the ancestral form, which was changed to a six-rowed spike in cultivated barley by mutation during domestication. In wild and cultivated barley the central spikelet is fertile and goes on to develop into a grain. The two lateral spikelets are sterile in the two-rowed type (wild and cultivated barley), but are fertile in six-rowed type (only cultivated barley). The fertile lateral spikelets that develop into grain appeared during barley domestication (Zohary, 1963; Bothmer *et al.*, 1995). In wild barley, the three spikelets form a light, arrowhead-like dispersal unit that both facilitates seed dispersal by animals and aids seed burial. The numerous upward-oriented barbs on the lemma and awn are also part of the dispersal and self-planting mechanisms. Reduced awn barbing seems important in its utilization as animal feed which is found in two-rowed cultivars. Six-rowed spontaneous mutants are not preferred for survival in the wild and they are eliminated naturally and rapidly from wild barley populations (Zohary, 1963; Bothmer *et al.*, 1995).

There are at least five independent loci controlling the six-rowed spike phenotype in barley. Six-rowed spike 1 (*vrs1*), a recessive gene located on chromosome 2HL (Fig. 2), is observed in all six-rowed cultivars. Wild barleys have dominant alleles for *Vrs1*, whereas cultivated barleys have a dominant *Vrs1* (two-rowed) allele or a recessive *vrs1* (six-rowed) allele depending on their phenotypic row-type. Cultivated barleys with recessive allele at *vrs1* are completely six-rowed over the whole spike (Lundqvist *et al.*, 1997). More than 90 mutant lines have been induced for this locus from two-rowed barley (Lundqvist *et al.*, 1997), which supports the hypothesis that six-rowed barley was derived from two-rowed barley by mutation. Allelic variation based on awn length development of lateral spikelets was observed among six-rowed barleys as *vrs1.a* and *vrs1.c*. In the *vrs1.a* allele, which exists in most of the six-rowed cultivars, awn lengths of lateral spikelets are nearly the same as the central spikelets (Fig. 3E; Lundqvist *et al.*, 1997). The *vrs1.c* allele is a six-rowed allele with awn-like appendages on the lemma of lateral spikelets (Lundqvist *et al.*, 1997). Two-rowed barleys also have different alleles of the *Vrs1.p* with pointed-tip lateral spikelets (Fig. 3D), *Vrs1.b* with round-tip lateral spikelets (Fig. 3B, C) and *Vrs1.t* with extremely rudimentary lateral spikelets (Fig. 3A). Analysis of a closely linked marker to *vrs1* suggested a hypothesis that six-rowed barley originated more than once in the history of barley domestication (Tanno *et al.*, 2002).

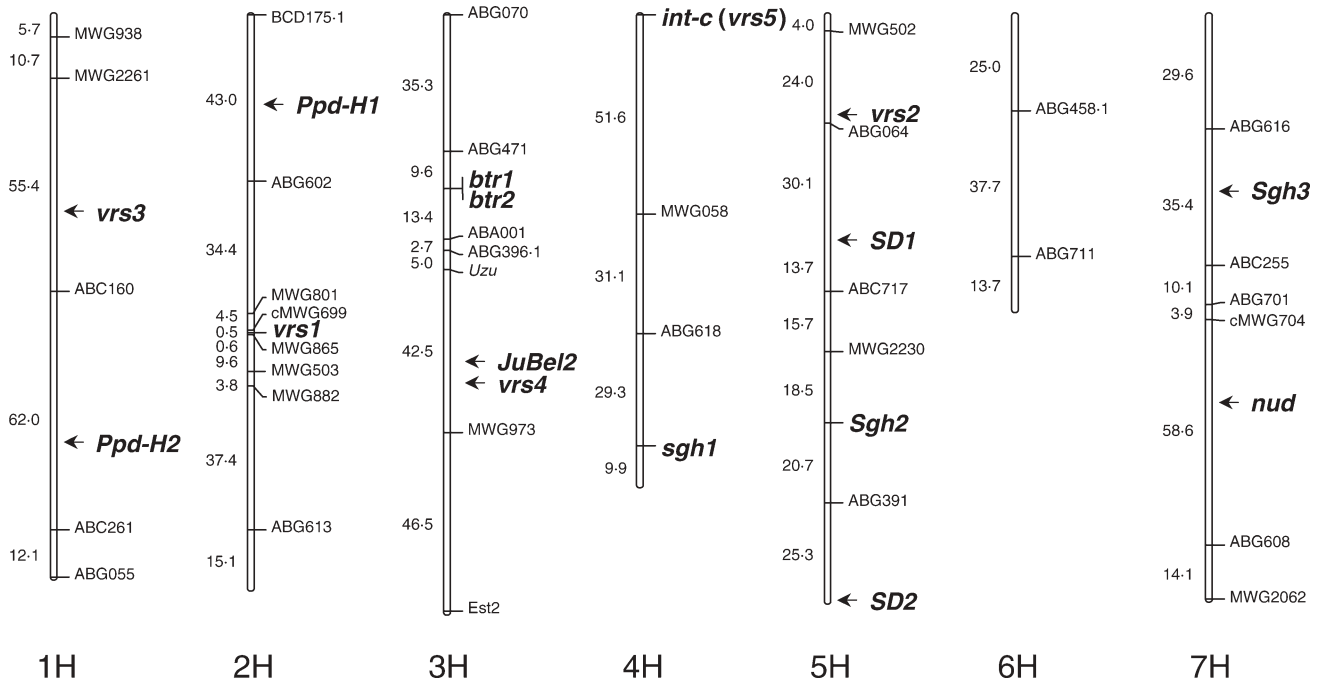


FIG. 2. Consensus map of barley domestication-related genes. RFLP markers from the cross Azumamugi × Kanto Nakate Gold (Mano *et al.*, 2001) were considered. Distances between markers are given in centimorgans. Genes were imposed on the genetic map by comparative mapping approach.


FIG. 3. Barley spikelets in one rachis node. (A) Ethiopian landrace var. *deficiens*; rudimentary lateral spikelets (*Vrs1.t*). (B) Wild barley var. *spontaneum*; sterile lateral spikelets (*Vrs1.b*). (C) Two-rowed cultivar var. *distichon*; sterile lateral spikelets (*Vrs1.b*). (D) Wild barley var. *proskowetzii*; short-awned or tip-pointed lateral spikelets (*Vrs1.p*). (E) Six-rowed cultivar convar. *vulgare*; fully fertile and awned lateral spikelets (*vrs1.a*).

Six-rowed spike 2 (*vrs2*), six-rowed spike 3 (*vrs3*) and six-rowed spike 4 (*vrs4*) are independent recessive genes, which are located on chromosome 5HL, 1HL and 3HL, respectively (Fig. 2; Lundqvist *et al.*, 1997). These loci are detected only in induced mutant lines and there are no reports of mutation in these loci in cultivars. Alleles at these loci enhance the development of lateral spikelets to various degrees depending on their position in the spike (Lundqvist *et al.*, 1997).

Six-rowed spike 5 (*vrs5* or *int-c*), a recessive gene located on chromosome 4HS, is detected in many two-rowed barley cultivars and more than 20 induced mutant lines (Lundqvist *et al.*, 1997). Alleles at the *int-c* locus modify the degree of fertility in lateral spikelets and produce an intermediate spike type. Of two alleles of this locus observed in cultivars, the *int-c.b* allele prevents anther development in lateral spikelets, whereas the *Int-c.h* allele allows the development of anthers and promotes occasional seed set in lateral spikelets (Leonard, 1942; Woodward, 1947; Lundqvist and Lundqvist, 1987). It remains to be determined whether the wild ancestor of domesticated barley had a dominant allele for *Int-c* or a dominant mutation created *Int-c* during domestication.

Among the five six-rowed spike loci only the natural mutation on *vrs1* and *vrs5*/*int-c* are observed in barley cultivars. Development of six-rowed barley is highly dependent on the evolution in these two genes. The effects of these two genes are opposite to each other in the sense that the dominant *Vrs1* allele suppresses the development of lateral spikelets but the dominant *Int-c.h* allele promotes development of lateral spikelets and occasional seed set. Because recessive *vrs1* is observed in all cultivated six-rowed barley cultivars, recessive mutation of this gene during barley domestication is the key point for the origin of six-rowed barley.

### *Naked caryopsis*

The hulled or naked caryopsis character of barley is an important agronomic trait because of its direct link to dietary use. Hulled barley has caryopses with the husk cemented to the grain, while naked barley grows with easily separable husks upon threshing. The remains of naked kernels have been found in Ali Kosh about 8000 BP which means a mutation for this trait occurred early in the domestication of barley (Helbaek, 1969). Harlan (1995) suggested that the change to non-brittle rachis preceded the emergence of naked caryopsis during the barley domestication. A single recessive gene, *nud*, located on chromosome 7HL (Fig. 2; Scholz, 1955; Fedak *et al.*, 1972), controls the naked caryopsis character, suggesting that easy separation of the husk results from a mutation that damaged gene function. Naked barley is distributed widely in the world, but there is a higher preference for naked barleys in East Asian countries such as China, Korea and Japan, and it is especially common in Tibet and the northern parts of Nepal, India and Pakistan (Bothmer *et al.*, 2003). Since the frequency is low in the Western countries, Vavilov (1926) considered southern Asia to be a centre of origin for naked barley. It has, however, become clear that naked barley was grown in Anatolia (Turkey) and in northern Europe in ancient times (Helbaek, 1969). The Naked gene has multiple effects on many traits of barley, like yield reduction and lower seed weight (Choo *et al.*, 2001).

Molecular analyses of a closely linked marker to the *nud* gene support the hypothesis of a monophyletic origin of this gene (Taketa *et al.*, 2004). This analysis clearly separated hulled, naked and wild barley into four alleles. One hundred naked cultivars have the same allele (monophyletic), and only one wild barley (OUH625, among 53 wild lines) from south-western Iran showed the same allele as the naked barley group. No hulled barley (among 106 cultivars) that carries same allele as a naked barley group. Taketa *et al.* (2004) hypothesized that naked barley originated from wild barley directly or it originated from hulled domesticated barley, which is now extinct. High-density and high-resolution mapping has delimited

the *nud* gene to a 0·66-cM region using AFLP markers (Kikuchi *et al.*, 2003; Taketa *et al.*, 2006). A BAC contig spanning the hulled or naked caryopsis locus (*Nud/nud*) with a length of 240 kb was made by chromosome walking (Amano *et al.*, 2006).

*Reduced dormancy*

Seed dormancy is defined as the temporary inability of a viable seed to germinate under favourable environmental conditions (Simpson, 1990). This trait enables seeds to survive adverse conditions and allows seed dispersal to a wider region (Snape *et al.*, 2001*b*). A high level of seed dormancy is a problem in cultivars when rapid seed germination on planting is needed. In the malthouse, seeds must germinate rapidly and completely upon imbibition of water, and a high level of dormancy after harvest is economically undesirable (Carn, 1980; Ullrich *et al.*, 1993, 1997). Nevertheless, stringent phenotypic selection against seed dormancy can lead to the development of barley cultivars susceptible to pre-harvest sprouting, which is also highly undesirable (Prada *et al.*, 2004). Generally, a moderate level of seed dormancy is thought to be appropriate for barley cultivars (Han *et al.*, 1999; Romagosa *et al.*, 1999).

Barley seed dormancy is a quantitative trait that is affected by several genes, environmental factors, and by gene × environment interactions (Ullrich *et al.*, 1996). Many seed dormancy QTLs have been identified in barley (Han *et al.*, 1996; Edney and Mather, 2004; Prada *et al.*, 2004; Zhang *et al.*, 2005; Vanhala and Stam, 2006). Cultivars of different pedigrees may have different dormancy genes, which explain the various QTL analysis results from different mapping populations. However, it is important to note that common major QTLs (*SD1*, *SD2*) have been identified in various studies (Li *et al.*, 2004).

*SD1* and *SD2* located at different loci on chromosome 5H (Fig. 2) are important in the study of seed dormancy. *SD1* has been detected as a major QTL near the centromere region on the long arm of chromosome 5H in most of the barley QTL mapping projects (Han *et al.*, 1996; Edney and Mather, 2004; Prada *et al.*, 2004; Zhang *et al.*, 2005). A single Mendelian gene controls the allele at *SD1* in which the dormancy allele is dominant. *SD1* shows the largest and most consistent effect on dormancy (Han *et al.*, 1999). This gene has been delimited to a 4·4-cM region in chromosome 5H (Han *et al.*, 1996, 1999). *SD2*, a region near the distal end of the long arm of chromosome 5H, has been detected as a QTL for seed dormancy (Takeda, 1996; Ullrich *et al.*, 1996). This gene controls a moderate level of seed dormancy, which makes it a promising candidate gene for utilization in barley breeding (Gao *et al.*, 2003). Fine mapping has resolved the *SD2* QTL to a 0·8-cM interval (Gao *et al.*, 2003). A gene coding for GA20-oxidase was identified as a candidate gene of *SD2* using barley–rice synteny (Li *et al.*, 2004), but its gene identity remains to be proven. *SD1* is epistatic to *SD2* at early-ripening stages, but they seem to act additively at later ripening stages (Romagosa *et al.*, 1999).

*Reduced vernalization requirement*

Vernalization is the requirement for a period of low temperature for a plant to make the transition from a vegetative to a reproductive state. The genes for the vernalization pathway prevent flower development during the winter, providing protection for floral organs against cold. One of the prerequisites for the expansion of barley production must have been development of a spring growth habit (no or reduced requirement for vernalization). Almost all wild barleys have a winter growth habit with the exception of a few strains which are regarded as hybrids with spring cultivars (Takahashi *et al.*, 1963, 1968). Both winter and spring barley are cultivated in mid-latitudinal regions including North Africa, southern Europe and Asia according to climate conditions. The development of barley lines lacking a vernalization requirement expanded barley cultivation to areas where spring sowing is necessary to avoid winter injury.

Three genes *sgh1*, *Sgh2* and *Sgh3* are detected in spring growth habit barleys and their allelic genes (*Sgh1*, *sgh2* and *sgh3*) are required for winter growth habit. Regarding the epistatic effects among these genes, only one genotype (*Sgh1sgh2sgh3*) showed winter growth habit. The multiple alleles of *Sgh2I* and *Sgh2II*, account for a gradation of vernalization requirements (Takahashi and Yasuda, 1956). Linkage analysis revealed the location of these spring growth habit genes on barley chromosomes 4H, 5H and 7H, respectively (Fig. 2; Takahashi and Yasuda, 1956, 1958; Yasuda, 1969; Laurie *et al.*, 1995; Yan *et al.*, 2006).

The first domesticated barleys are likely to have had a winter growth habit. Later a dominant mutation occurred in the *sgh2* locus, resulting in spring barley of *Sgh1Sgh2sgh3* (type I) (Takahashi *et al.*, 1963, 1968). The *Sgh2* mutation occurred many times independently based on molecular analysis of the gene region (Ohmura *et al.*, 2006). Subsequently, mutations from *Sgh1* and *sgh3* might have occurred independently in type I, because both *sgh1* and *Sgh3* spring genes are mostly associated with *Sgh2*. Other genotypes are supposed to be hybrids (Takahashi *et al.*, 1963, 1968; Bothmer *et al.*, 2003), but the multiple origin of *Sgh2* implies a more complex story. These three genes have also been called in barley *Vrn-H1* (corresponding to *Sgh2*), *Vrn-H2* (corresponding to *Sgh1*) and *Vrn-H3* (corresponding to *Sgh3*). Similar epistatic interactions and map locations indicate that barley and wheat vernalization genes are orthologous (Laurie *et al.*, 1995; Dubcovsky *et al.*, 1998; Yan *et al.*, 2004), and wheat *VRN1* (orthologue of barley *Sgh2*), *VRN2* (orthologue of barley *Sgh1*) and *VRN3* (orthologue of barley *Sgh3*) were isolated by positional cloning (Yan *et al.*, 2003, 2004, 2006).

Both *Sgh2* and *VRN1* are dominant for spring growth habit. The wheat *VRN1* gene is an *APETALA1* gene of the MADS-box gene family, which initiates the transition from the vegetative to reproductive apex (Yan *et al.*, 2003). Both *Sgh1* and *VRN2* are dominant for winter growth habit. Wheat *VRN2* encodes zinc finger in the first exon and the CCT domain in the second exon (called *ZCCT1*), which inhibits the transition of plants from the vegetative to reproductive stage (Yan *et al.*, 2004). Transcription of

this gene is gradually down-regulated by vernalization. Therefore wheat *VRN1* and *VRN2* have opposite transcription profiles. Southern blot analysis of barley genomic DNA using wheat *ZCCT1* as a probe in 85 barley cultivars showed the presence of this gene in 23 winter barley lines and deletion of this gene in 62 spring barley lines (Yan *et al.*, 2004). Both barley *Sgh3* and wheat *VRN3* are dominant for spring growth habit. These genes are *FLOWERING LOCUS T* (*FT*) orthologues and were isolated from rice and arabidopsis related to flowering time (Yan *et al.*, 2006, and references cited therein). The dominant allele with a high level of transcript shows early flowering in barley and wheat. Based on the tentative model present by Yan *et al.* (2006), *VRN2* negatively regulates *VRN1* and *VRN3* and *VRN2* is down-regulated by vernalization. First intron of *Vrn-H1* may include an intronic regulatory element for the flowering repressor mediated by *Vrn-H2* gene products of barley (Fu *et al*., 2005).

In barley, photoperiod has an important main effect and interactive role with vernalization in determining flowering time (Karsai *et al.*, 2005; Trevaskis *et al.*, 2006). Vernalization and photoperiod sensitivity may contribute to low temperature tolerance by maintaining plants in a vegetative state and expression of low temperature tolerance genes (Karsai *et al.*, 2001; Mahfoozi *et al.*, 2001).

### *Photoperiod insensitivity*

Plants have evolved to ensure that flowering occurs when there is the greatest chance of pollination, seed development and seed dispersal. These constraints apply to wild ancestors, but the modification of flowering time by human selection has been essential to the spread of barley worldwide.

In barley, flowering time is a highly variable phenotypic trait with major implications for adaptation to geographic regions (Calder, 1965). This physiological trait is controlled by many genes including photoperiod response genes (Laurie, 1997). Plant growth and development, including photoperiod-dependent flowering, is regulated by the products of the red/far-red light phytochrome and the blue/UV-A light cryptochrome photoreceptor gene families (Cashmore *et al.*, 1999; Lin, 2000; Quail, 2002). Wild barley has been classified as a quantitative long-day (LD) species, implying that the heading time is advanced by increasing day length (Boyd *et al.*, 2003). Spring barley accumulated LD-insensitive mutants to allow an extended vegetative growth period under LD. This is likely to have favoured expansion of the barley production area into higher latitudes.

The major determinant of LD response in barley is the *Ppd-H1* locus located on chromosome 2HS (Fig. 2; Laurie *et al.*, 1995; Karsai *et al.*, 1997; Decousset *et al.*, 2000). Wild barleys have a dominant allele at the *Ppd-H1* locus, while cultivated barleys can be divided into two groups either having or lacking the dominant allele. *Ppd-H1* plants head about 20 d earlier than *ppd-H1* plants under LD conditions (16 h of light) (Turner *et al.*, 2005). The recessive nature of photoperiod-insensitive, *ppd-H1*, suggests that reduced response results from a mutation that impairs gene function. Cross-hybridizing markers show that *Ppd-H1* can be homoeologous to the wheat *Ppd-1* series of genes on chromosome group 2 of wheat (Snape *et al.*, 2001*a*). Cloning of *Ppd-H1* (Turner *et al.*, 2005) revealed a pseudo-response regulator (PRR) which is different from the major rice photoperiod response genes, *Hd1* and *Hd3a* (Yano *et al.*, 2000; Kojima *et al.*, 2002) but is likely to be orthologous to rice *Hd2* (OsPRR37; Murakami *et al.*, 2005). Significant pleiotropic effects of the *Ppd-H1* locus under LD on plant height, plant yield, tiller yield, spike length and grain number per tiller were detected (Laurie *et al.*, 1994; Sameri *et al.*, 2006). In all cases, presence of the photoperiod-insensitive allele resulted in higher values. A second major photoperiod response gene, *Ppd-H2*, has been mapped on the long arm of the chromosome 1H (Fig. 2). Explicit differences in flowering time under short days (10 h) were observed, but *Ppd-H2* has little effect under long days (13–16 h) (Laurie *et al.*, 1995; Szücs *et al.*, 2006). Genes and mutants at $>14$ other loci have been associated with earliness in barley (Lundqvist *et al.*, 1997). These genes in various combinations permit plant breeders to adapt barley for production in many parts of the world.

## ISOLATION OF SIX-ROWED SPIKE 1, *VRS1* GENE

Elucidation of the origin of six-rowed barley has been a long-term goal of barley scientists. Helbaek (1959) hypothesized that six-rowed barley originated from two-rowed cultivated barley based on archaeological evidence. Tanno *et al.* (2002) proposed that six-rowed barley had two different origins based on sequence analysis of a closely linked DNA marker to *vrs1*. Isolation of the *vrs1* gene is crucial for testing these hypotheses.

To clone *vrs1*, the six-rowed spike gene was delimited to 1 cM using STSs derived from RFLP and AFLP markers (Komatsuda *et al.*, 1998, 1999; He *et al.*, 2004). Comparison of six high-resolution maps using different parents revealed that marker order around the *vrs1* gene is constant and there is no drastic rearrangement among barley cultivars in this region (Komatsuda and Tanno, 2004). After long-term gene mapping efforts, a barley–rice synteny approach was used taking advantage of the complete rice genomic sequence (International Rice Genome Sequencing Project, 2005) and extensive available barley ESTs in public databases for marker enrichment. This strategy enabled *vrs1* to be delimited to 0·06 cM (Pourkheirandish *et al.*, 2007). The *vrs1* gene was isolated by means of positional cloning (Komatsuda *et al.*, 2007). A BAC contig spanning the *vrs1* locus with a length of 518 kb was made by chromosome walking. Cloning of the *vrs1* gene revealed that *Vrs1* encodes a member of the homeodomain-leucine zipper (HD-ZIP) I class of transcription factors. The dominant nature of *Vrs1* suggests VRS1 is a repressor protein that binds to the DNA of genes and regulates the development of lateral spikelets as a transcription factor. The result agrees with the theory of Doebley (2006) that most domestication genes involve changes to transcription factors.

Analysis of induced mutants from two-rowed barley (Komatsuda *et al.*, 2007) revealed that loss of function of *Vrs1* caused six-rowed or intermediate phenotypes in mutant spikes. The functional character of *Vrs1* in

two-rowed barley agrees with the hypothesis of Helbaek (1969) based on archaeological evidence that six-rowed barley originated from two-rowed barley. This result also confirmed that two-rowed barley is the ancestral form of barley. *In situ* hybridization of *Vrs1* revealed that this gene is expressed only in lateral spikelets at the immature stage (Komatsuda *et al.*, 2007), which is the reason that this gene only affects the development of lateral spikelets. Sequence analysis of the *vrs1* gene among a worldwide collection of six-rowed cultivars revealed three independent origins for six-rowed barley. Two of them (alleles *vrs1.a2* and *vrs1.a3*) were derived from their immediate ancestor two-rowed cultivated barley (alleles *Vrs1.b2* and *Vrs1.b3* Fig. 3C) by a single nucleotide mutation. This result agrees with the hypothesis of Tanno *et al.* (2002) that six-rowed barley originated more than once during barley domestication. The origin of *vrs1.a1*, the most widespread allele and probably the first allele of six-rowed barley, was not found among two-rowed cultivars tested in the study (Komatsuda *et al.*, 2007). It remains to be determined whether this six-rowed allele was derived from extinct two-rowed cultivated barley or it is directly derived from wild barley and then outcrossing with non-brittle lines resulted in six-rowed cultivars with the *vrs1.a1* allele. To answer this question, sequence analysis of *vrs1* among a worldwide collection of wild barleys would be useful.

Characterization of a 518-kb barley contig harbouring the *vrs1* gene revealed that the six-rowed spike 1 gene is located in a gene poor-region (Pourkheirandish *et al.*, 2007). Recombination was highly suppressed around the *vrs1* gene in this contig. Comparison of the barley *vrs1* contig and rice genome sequence revealed that the rice orthologue of *vrs1* (*Oshox14*) is located in rice chromosome 7 instead of a collinear region in rice chromosome 4. This result suggests that a translocation occurred in barley or rice during evolution.

## CONCLUSIONS

The above review shows the importance of understanding on genes related to crop domestication and migration. Crop domestication and migration made agriculture efficient, which was the critical stage in development of human civilizations (Salamini *et al.*, 2002). It is hypothesized that changing climate might have lead to communities cultivating wild plants in a limited area to survive and that was the starting point of human agriculture (Salamini *et al.*, 2002). The precise time/s when and region/s where barley domestication occurred are not entirely known. The *vrs1* gene affects the visual yield of barley because plants have three times as many seeds per spike as two-rowed plants. The study of isolated alleles at the six-rowed spike locus has resulted in a leap in the understanding of barley domestication. To further elucidate the story of barley domestication, it will be necessary to isolate and study critical genes such as non-brittle rachis (*btr1* and *btr2*) and naked caryopsis (*nud*).

Each cereal crop is derived from a single common ancestor (Moore, 1995). Based on the assumption of Moore (1995) different crops should carry the same genes derived from their common ancestor. The grass family emerged approx. 60 million years ago and the Triticeae diverged approx. 12 million years ago (Devos, 2005). Traits are controlled by a number of genes located in different genetic loci, acting as a network within the cell. These networks are inherited from a common ancestor of crops. The ancestors of crops diverged from each other millions of years ago, but domestication was initiated about 10 000 BP. Thus, different mutations during domestication may have targeted different genes from the same network corresponding to a single trait in different crops. For example, isolation of photoperiod-response genes in barley and rice revealed that the mechanism of photoperiod response was inherited from a common ancestor in barley and rice, but different mutations targeted different genes during evolution after separation of barley and rice (Turner *et al.*, 2005). Most of the domestication genes isolated so far are transcription factors (Doebley, 2006). The regulatory genes, which control the expression of structural genes in target tissue at specific developmental stages, may evolve to control different genes downstream from these regulatory genes in different crops. Even though some regulatory elements are orthologues in different crops, it is possible that these orthologue elements interfere with different responses. Most of the domestication traits are the result of a mutation that leads to a loss of function (Doebley, 2006). The *vrs1* locus has a unique function in barley that controls the development of lateral spikelets. This function may not exist in the other cereals like wheat or rice because of their inflorescence structure. Comparison of barley and rice for *vrs1* revealed that, even though an *vrs1* orthologue exists in rice, it is not in a collinear location with barley, which revealed an evolutionary rearrangement. This rearrangement may relate to a special function of this gene in barley.

## ACKNOWLEDGMENTS

We thank Dr S. Taketa, Dr S. Nakamura, Dr K. Kato and Dr D. Vaughan for comments on the manuscript. The financial support from the Ministry of Agriculture, Forestry and Fisheries of Japan (Rice Genome Project MP1113b and Green Techno Project GD3006) and research grant of CREST program of Japan Science and Technology Agency (JST) to T. Komatsuda are gratefully acknowledged. Funding to pay the Open Access publication charges for this article was provided by the OECD.

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