11 Genomic Insights on Global Journeys of Adaptive Wheat Genes that Brought Us to Modern Wheat

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Abstract

Since its first cultivation, hexaploid wheat has evolved, allowing for its widespread cultivation and contributing to global food security. The identification of adaptive genes, such as vernalization and photoperiod response genes, has played a crucial role in optimizing wheat production, being instrumental in fine-tuning flowering and reproductive cycles in response to changing climates and evolving agricultural practices. While these adaptive genes have expanded the range of variation suitable for adaptation, further research is needed to understand their mechanisms, dissect the pathways involved, and expedite their implementation in breeding programs. By analyzing data across different environments and over time, Meta-QTL analysis can help identify novel genomic regions and facilitate the discovery of new candidate genes. This chapter reports on two previously unknown Meta-QTL regions, highlighting the potential for further exploration in this field. Moving forward, it will be increasingly important to expand our understanding of how genetic regions influence not only flowering time but also other developmental traits and their responses to environmental factors. Advances in gene-based modeling hold promise for describing growth and development processes using QTL and other genomic loci analysis. Integrating these findings into process-based crop models can provide valuable insights for future research. Overall, the study of adaptive genes and their

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impact on wheat production represents a vital area of research that continues to contribute to global food security.

Keywords

Hexaploid wheat · Adaptive genes · Novel genomic regions · QTL · Gene-based modeling · Process-based modeling · Global food security

11.1 Historical Perspective

Archaeological evidence suggests that hexaploid wheat was first cultivated in the Fertile Crescent of the Middle East around 7000 BC and that farming spread to Europe (former Yugoslavia, Bulgaria, Greece) approximately one thousand years later (Hillman 1972; Renfrew 1973). By approximately 4000 BC, wheat production had reached China, with archeological isotope analysis suggesting diets shifted from a dominance of C4 crop millet, to C3 cereals including wheat (Li et al. 2007; Cheung et al. 2019). The coincidence of changing climate, whereby conditions became colder and drier, is proposed to have led to the adoption of wheat due to its greater flexibility in sowing time to achieve yield (Cheung et al. 2019). The ancient Greek poet Hesiod described an awareness of the importance of the seasonal timing of wheat development as early as 800 BC in Greece (Aitken 1974), and approximately two thousand years later, French scientist Réaumur constructed a thermometer and showed that crop maturity was influenced by temperature (Réaumur 1735). In 1751 Carl von Linné published a floral calendar in Philosophia Botanica, observing that plant responses to the environment varied in different climates (Linné and Freer 2007), and since this time, multiple evidence of variation in flowering time due to temperature, daylength, and latitude has been reported (Aitken 1974). From the eighteenth century, bread wheat (*Triticum aestivum* L.) has grown on all continents except Antarctica, and to ensure successful cultivation in different environments, wheat breeding (hybridization and selection to achieve adaptation) began.

11.1.1 Early Breeding and Selection for Seasonal Adaptation

In France in 1743, the seed merchant Jeanne Claude Geoffroy and botanist Pierre d'Andrieux founded a seed company which began the Vilmorin family dynasty of wheat breeding that lasted more than 200 years. There is evidence that pedigree-based breeding was used at the Vilmorin company from 1840, with selection of seeds based on evaluation of progeny performance (Gayon and Zallen 1998). Henry de Vilmorin described the importance of wheat adaptation in Les meillieurs bles ("The best wheat") which illustrated the morphology, origin, adaptation, and best agronomic practice for different varieties. His astute preface included, "one of the best ways to increase harvests without increasing expenditure is to cultivate the breeds of wheat which are best suited to the circumstances in which the land is cultivated" and to "choose knowingly the most advantageous wheat in each locality" (Vilmorin 1880). Vilmorin had begun hybridization experiments in 1873, including the use of wheat which had been selected by Scottish agriculturalist Patrick Shirreff (Vilmorin 1880). Vilmorin's first variety DATTEL released 10 years later was the result of crossing an early maturing, short stature type from France with late maturing English wheat. DATTEL became widely adopted, as resistance to lodging and earliness created a uniform crop with high yield potential. A string of successful cultivars followed including VILMORIN 23, VILMORIN 27, and VILMORIN 29 and many others which feature in the ancestry of modern wheat (Lupton 1987).

At approximately the same time another European breeder, Wilhelm Rimpau was also crossing native types to English Squarehead wheat for improved yield, using North American varieties as donors of quality and winter hardiness. His most successful cultivar RIMPAU'S FRÜHER BASTARD was the most widely

grown in Germany for over 50 years after being released in 1889 (Porsche and Taylor 2001). That same year, pioneer breeder William Farrer made his first wheat crosses in Australia. Farrer also focused on introgression of wheat to improve quality and adaptation. He crossed European Purple Straw with Canadian Fife and Indian wheat, and the resulting early maturing cultivars were successful in Australia because the short life cycle avoided water-limiting conditions in summer and escaped rust infection. Farrer cultivars went on to dominate Australian wheat production in the early 1900s, on the basis that "He recognized that the characteristics of a variety limited its successful growth to certain localities, and therefore set himself the task of breeding varieties adapted to the different conditions" (Guthrie 1922).

The Canadian "hard" wheat FIFE used for crossing by Farrer created cultivars with increased dough strength relative to the soft white wheats traditionally used for baking. Initially, Farrer wheat was met with resistance from millers. From the Rust in Wheat Conference in Melbourne, 1896, "A prominent obstacle this Conference has met with has arisen from the objection of millers. The opinion this Conference has long held is that the opposition of millers to such wheats has no legitimate foundation but arises from either misconception or from conservatism" (Guthrie 1922). Australian millers realized the superior quality of Farrer wheat only when American wheat of the same type was imported to Australia to meet local demand (Guthrie 1922).

Other breeders were also crossing Canadian FIFE and INDIAN wheat. In Canada, Percy Saunders crossed RED FIFE and HARD RED CALCUTTA, and the resulting cultivar MARQUIS was selected and released by Charles Saunders in 1908. With excellent quality and adaptation through early maturity, MARQUIS dominated Canadian production and became the gold standard for quality classification (Lupton 1987; McCallum and DePauw 2008). The overwhelming popularity of MARQUIS (and two later releases, THATCHER and NEEPAWA) highlights a negative consequence if few adapted cultivars are widely used, that is, a decline of genetic diversity in the breeding pool over time (Fu and Dong 2015).

11.1.2 Expanding Knowledge of Seasonal Patterns

Fluctuating patterns of seasonal flowering time have been well documented across plant species (Andrés and Coupland 2012). Early work by Garner and Allard (1920) described the relationship between daily light duration, plant growth, and reproduction across several plant species. Their work demonstrated that daily light duration impacted both the rate and extent of growth as well as the time to reach and complete flowering and reproduction (Garner and Allard 1920). In wheat, Chinoy (1950) demonstrated that long days induced earlier onset of the reproductive phase with both cold (vernalization) and light (photoperiod) having measurable impact on development and growth. It was proposed that the first wheat (which were domesticated in the Fertile Crescent) shared both vernalization requirements and photoperiod responses with their progenitors, but that selection for alternative adaptation facilitated the spread of wheat throughout Europe, and then worldwide (reviewed by Cockram et al. 2007).

The detection of major genes controlling vernalization (positive vernalization response from wheat variety INSIGNIA 49 (Pugsley 1963)) and photoperiod (from Canadian variety SELKIRK (Pugsley 1965)) was demonstrated in segregating populations and provided evidence for simple inheritance. This offered the opportunity to apply selection for daylength specificity (Pugsley 1965), although additional genetic controllers were hypothesized. Genes for daylength duration, *Photoperiod-1* (*PPD1*), were mapped to the homoeologous group 2 chromosomes (Law et al. 1978) and studies by Martinic (1975) and Hunt (1979) demonstrated the prevalence of photoperiod-sensitive winter wheat in northern latitudes and photoperiod insensitivity in southern Europe.

Creation of near-isogenic wheat lines capturing *PPD1* variation by Worland and Law (1986) and Worland et al. (1998) confirmed genetic effects and allowed the understanding of their environmental performance throughout Europe. This demonstrated a yield disadvantage from earlier flowering in the UK, a moderate advantage in Germany, and a significant advantage in southern Europe (based on testing in the former Yugoslavia). These effects have been further elaborated with Börner et al. (1993) confirming that middle European varieties benefit from daylength sensitivity (conferred by *PPD1*), whereas insensitivity offers productivity-related increases where wheat experiences hot and dry summer conditions. Hoogendoorn (1985) assessed phenotypic response to photoperiod and vernalization in a collection of 33 wheat varieties from a range of geographies. This confirmed a prevalence of photoperiod sensitivity in varieties from Europe and North America and insensitivity in varieties originating from Mexico, India, and Australia.

Since the development of understanding the major controllers of photoperiod response and vernalization requirements in wheat, variation for the *PPD1* and *Vernalization-1* (*VRN1)* genes has aided wheat's adaptation to a wide range of global production environments (Sheehan and Bentley 2020). In many geographies, there is a documented progression of wheat cultivation across climatic features and areas including in North America (Olmstead and Rhode 2011), Asia, the Mediterranean, North Africa (Ortiz Ferrara et al. 1998), and China (Yang et al 2009).

11.1.3 Further Adaptive Progress Through Time

Farrer was first to target early maturity to breed adapted wheat for Australia, although the introduction of additional genetic diversity for phenology had been identified (Eagles et al. 2009). In 1945, Australian breeder Walter Lawry Waterhouse introgressed hexaploid wheat and an early maturing durum wheat, GAZA, producing an important cultivar, GABO. This daylength insensitive wheat was the leading cultivar in Australia for many years and sister line TIMSTEIN was also successfully cultivated in USA. This germplasm was utilized by the International Maize and Wheat Improvement Center (CIMMYT) in the breeding of cultivars such as CAJEME, MAYO, and NAINARI (Watson and Frankel 1972).

Other donors of photoperiod insensitivity have been traced to Japanese landrace AKAGOMUGHI (which also carried dwarfing gene, *RHT8*) and Chinese landraces MAZHAMAI and YOUZIMAI (Yang et al. 2009). Yang et al. (2009) showed that the distribution of alleles for daylength sensitivity depended upon the climate (temperature and latitude) where the wheat was cultivated. The adoption of photoperiod insensitive wheat by CIMMYT was key to the success of the shuttle-breeding program, whereby material could undergo selection in multiple environments due to broad adaptation (Trethowan et al. 2007). It is the subsequent sharing of germplasm during the "Green Revolution" which likely facilitated the spread of alleles for daylength insensitivity around the globe.

As the climate changes over time and new crop management practices are developed, it is probable that new genetic variation will be required for enhancing adaptation (Hunt et al. 2019). For instance, studies have highlighted a shift to early sowing which has meant that vernalization responsive, long season wheat are beneficial in some areas of southern Australia where spring types are traditionally cultivated (Hunt 2017; Cann et al. 2020). To expedite development of future adapted wheat cultivars, it is important to understand the genetic architecture of phenology and develop breeding tools such as molecular markers and simulation models for prediction.

11.2 Understanding the Genetic Control of the Synchrony of Flowering

11.2.1 The Three Known Gene Systems

As outlined above, within less than 10,000 years, wheat cultivation has expanded from its primary area of evolution within the Fertile Crescent to a broad spectrum of agro-ecology around the globe, adapting rapidly to a wide range of climatic conditions (Curtis 2002; Salamini et al. 2002). The essential path to achieve adaptation is the synchrony of flowering which in wheat is controlled by three major gene systems: (1) the *VRN* genes (exposure to cold temperature), (2) the *PPD* response genes (sensitivity to daylength), and (3) the autonomous earliness per se (*EPS*) genes (Kato and Yanagata 1988). The adaptation of a wheat genotype to a particular environment depends to a large extent on the interaction of these three systems.

11.2.2 Vernalization (VRN) Genes

Vernalization is the acquisition of a plant's ability to flower by exposure to cold (Chouard 1960). According to the vernalization requirement of a genotype, wheat is classified as having a winter or spring growth habit. Winter wheat has a considerable vernalization requirement, but spring wheat may be insensitive or only partly sensitive to vernalization (Trevaskis et al. 2003). The key element of the vernalization gene system is *VRN1* with its three orthologous genes (*VRN-A1*, *VRN-B1*, and *VRN-D1*) located on the long arms of chromosomes 5A, 5B, and 5D, respectively (Figs. 11.1 and 11.2a). *VRN1* is a member of the MADS-box transcription factor family, which has been shown to play a critical role in flowering gene models across crops (Zhao et al. 2006). The MIKC-type MADS-box proteins have a highly conserved MADS DNA-binding domain, an intervening (I) domain, a keratin-like (K) domain, and a C-terminal domain (C). The proteins bind as dimers to DNA sequences named "CArG" boxes and organize in tetrameric complexes (Li et al. 2019). The multimeric nature of these complexes generates many combinatorial possibilities with different targets and functions (Li et al. 2019; Honma and Goto 2001; Theißen et al. 2016).

Mutations in the promoter and deletions in the large first intron of *VRN1* are associated with increased expression of the genes in the absence of cold, accelerated flowering without vernalization and thus spring growth habit (Kippes et al. 2018). Additionally, single nucleotide polymorphisms (SNPs) in exons 4 and 7 have been identified in *VRN-A1* (Eagles et al. 2011; Muterko and Salina 2018). The exon 4 SNP results in an amino acid change (Leu117 → Phe117) in the conserved k-domain (Eagles et al. 2011; Chen et al. 2009; Díaz et al. 2012). This polymorphism was associated with a change in the number of days to stem elongation, vernalization requirement duration, frost tolerance, and flowering time in winter wheat (Chen et al. 2009; Muterko et al. 2016; Dixon et al. 2019). Another *VRN-A1* SNP that causes an amino acid substitution (Ala180 → Val180) in exon 7 in the C-terminal domain also regulates vernalization duration, via its regulation of a protein interaction with *TaHOX1* (Li et al. 2013).

Beyond regulation by alterations in nucleotide sequence (INDELS and SNPs), there is increasing evidence that vernalization in wheat is also regulated at the epigenetic level. The *VRN-A1* gene can be present as two or more copies with the assumption that the number of copies positively correlates with the vernalization requirement duration and flowering time of wheat (Díaz et al. 2012). The different nature of the diverse mutations (promoter insertions, intron deletions of different size, SNPs) in the three *VRN1* orthologs and gene duplication in the A genome are the most plausible explanation for varying gene actions observed (Li et al. 2013). Dominant alleles at *VRN-A1* have been shown to confer the largest effects leading to a lack of vernalization requirement relative to

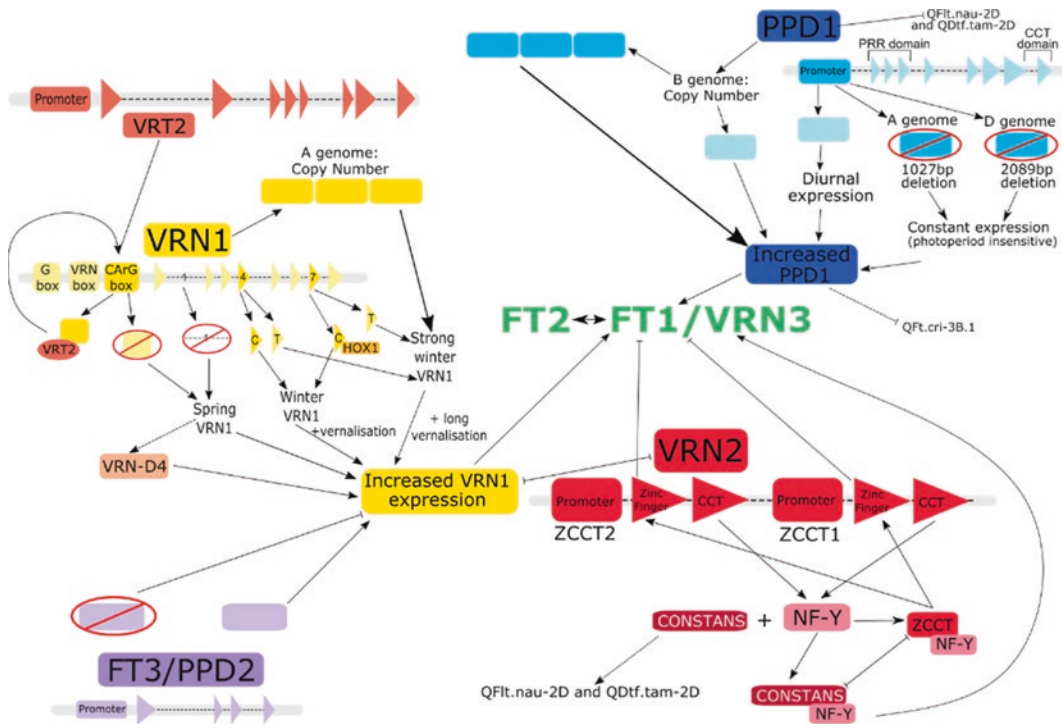

Fig. 11.1 Major flowering genes involved in photoperiod and vernalization response. The major genes involved with photoperiod and vernalization responses in wheat are highlighted in different colors. For each gene, known allelic variation is included and the effect of this variation on the level of expression or the flowering response is shown. The structure of each gene, along with the annotated domains, is represented on a gray background bar. Where interactions with uncharacterized QTL regions are known, these are also included on the network diagram. Deletions are indicated by a red oval with a line through it. Different *VRN1* alleles can determine the extent to which vernalization is required to increase expression, due to CArG box, *VRT2* interactions, and exon variants, including changes in copy number. A duplication and translocation of *VRN1*, in the form of *VRN-D4*, also promote spring habit. The locus *VRN2* (*ZCCT1* and *ZCCT2*) is a photoperiod-dependent repressor of *VRN1*, competing with CONSTANS and the nuclear transcription factor Y (NF-Y) proteins to activate *FT1* (also called *VRN3*) and potentially *FT2*. The *FT* genes interact with FD-like genes (*FDL2* or *FDL12*) to form a floral activating complex. Copy number variants, most notably of *VRN1* and *PPD1*, can determine heading date. *PPD1* determines flowering time through photoperiod sensitivity with variations in promoter deletions and copy number influencing expression levels. Short-day promotion of flowering is mediated through FT3 (also called PPD-2)

VRN-B1 and *VRN-D1*, which reduced vernalization requirement and defined semi-spring or facultative types (Trevaskis et al. 2003).

Other MADS-box genes also play a role in the regulation of wheat flowering. *VRN-D4* is a MADS-box transcription factor derived from the duplication and translocation of the *VRN-A1* gene to the short arm of chromosome 5D (Kippes et al. 2015). Being an extra gene copy, *VRN-D4* is associated with increased *VRN-A1* expression and thus reduced vernalization requirement. The *VEGETATIVE TO REPRODUCTIVE TRANSITION 2* (*VRT2*) gene belongs to the group of MADS-genes as *SHORT VEGETATIVE PHASE* in Arabidopsis and interacts with *VRN1*. The *VRT2* protein has been shown to bind to the CArG box in the *VRN1* promoter region, suggesting that *VRT2* represses the transcription of *VRN1* (Dubcovsky et al. 2008; Kane et al. 2007). More recently, Xie et al. (2021) corroborated an epistatic interaction between the two genes (including the ability of *VRT2* to bind to the promoter region of *VRN1*), but reported a shared upregulation of *VRN1* and *VRT2*.

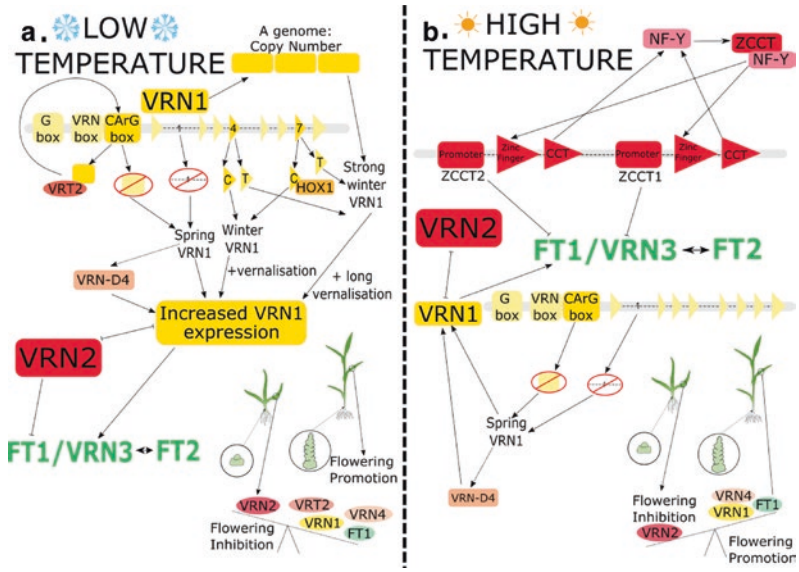

Fig. 11.2 Impact of major flowering genes responses to different temperatures, in the context of vernalization. This figure represents the role of temperature in the regulation of vegetative to reproductive meristem transition, and how this relates to the vernalization pathway. To indicate the different aspects of the flowering pathway and how responses which occur are more influenced by specific environmental conditions the pathway has been separated into **a** low temperatures and **b** high temperature (post or non-requiring vernalization), although it must be emphasized that each aspect does not act independently. The same gene structure and nomenclature are used as for Fig. 11.1. Additionally, the weighting of each gene signal is indicated in a seesaw schematic (see also Fig. 11.4)

In addition to *VRN1*, the *VRN2* and *VRN3* genes are located on the long arm of chromosome 5A and the short arm of chromosome 7B, respectively (Figs. 11.1 and 11.2). The *VRN*2 locus consists of two closely related genes (*ZCCT1* and *ZCCT2*) that encode proteins carrying a putative zinc finger and a CCT domain (Yan et al. 2004). The CCT domain is a 43-amino acid region, first described in protein sequences of CONSTANS (CO), CONSTANS-like (COL), and TIMING OF CAB1 (TOC1) (Putterill et al. 1995; Strayer et al. 2000; Robson et al. 2001) that is present in multiple regulatory proteins associated with light signaling, circadian rhythms, and photoperiodic flowering (Wenkel et al. 2006). *VRN2* is the major flowering repressor identified in wheat. Dominant gene action in combination with recessive *VRN1* and *VRN3* allele combinations confers winter wheat growth habit. Deletions or mutations involving positively charged amino acids at the CCT domain are associated with recessive *ZCCT1* and *ZCCT2* alleles for spring growth habit (Yan et al. 2004; Dubcovsky et al. 2005; Distelfeld et al. 2009). The CCT domains in ZCCT1, ZCCT2, and CO proteins further interact with proteins of the NUCLEAR FACTOR-Y (NF-Y) transcription factor family. Mutations in the CCT domain of ZCCT proteins also reduce the strength of ZCCT-NF-Y interactions and the ability of ZCCT1 to compete with CO to activate *VRN3* (Figs. 11.1 and 11.2b).

The *VRN3* gene encodes a RAF kinase inhibitor-like protein and has been mapped to the *FLOWERING LOCUS T-like* gene, often referred to as *FT1* in wheat. *VRN3/FT1* is expressed in long days in vernalized plants or spring types and thus triggers long-day-induced flowering. The VRN3/FT1 protein has been shown to travel through the phloem carrying the photoperiodic signal from the leaves to the shoot apex where it forms a protein complex binding to the promoter of *VRN1*, promoting its further expression. Dubcovsky et al. (2008)

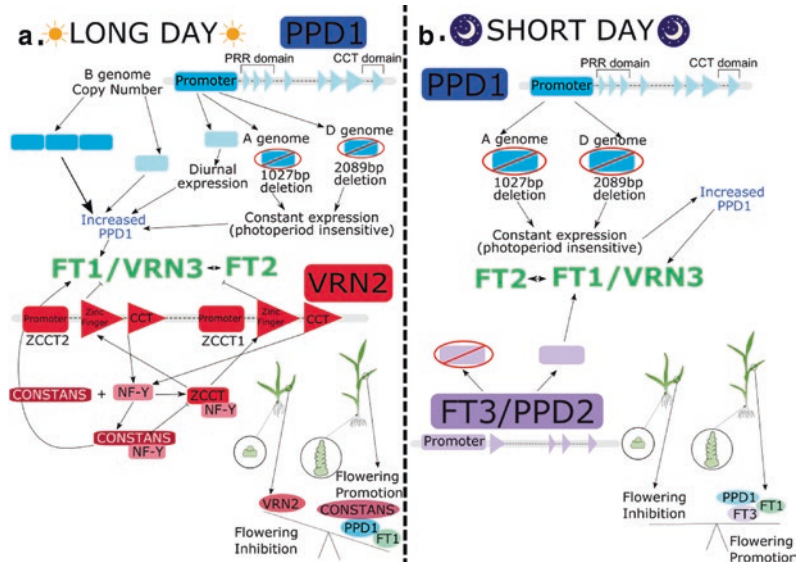

Fig. 11.3 Impact of major flowering genes responses to different daylengths. The role of daylength is represented in the regulation of vegetative to reproductive meristem transition. To indicate the different aspects of the flowering pathway and how responses which occur are more influenced by specific environmental conditions, the pathway has been separated into **a** long-day, **b** short-day, although it must be emphasized that each aspect does not act independently. The same gene structure and nomenclature are used as for Fig. 11.1. Additionally, the weighting of each gene signal is indicated in a seesaw schematic (see also Fig. 11.4)

demonstrated interaction of *Vrn3*/*FT1* with the FT2, FDL2, and FDL13 proteins. Transgenic plants showed that increased transcript levels of *FT2* (a *FT* paralogue) provide transcriptional activation of *VRN1*. *VRN3/FT1* therefore integrates the vernalization and photoperiod response gene systems. High levels of *VRN3/FT1* expression can overcome the vernalization requirement and are associated with spring growth habit (Figs. 11.1 and 11.2b) (Yan et al. 2006).

11.2.3 Photoperiod (PPD) Response Genes

Photoperiod genes promote the floral transition in response to long days (Searle and Coupland 2004). Photoperiod-sensitive wheat has a long-day phenotype. They flower earlier when the days are longer than a critical threshold. Photoperiod-insensitive wheat flowers largely independently of daylength and can be grown to maturity in long- or short-day environments. Photoperiod response is mainly controlled by the semi-dominant homoeologous *PPD1* genes on the short arm of chromosome group 2 (Law et al. 1978; Welsh et al. 1973). *PPD1* belongs to a pseudo-response regulator (*PRR*) gene family, which is characterized by a pseudo-receiver domain near the amino-terminus and a 43 amino acid CCT domain near the carboxy-terminus of the protein (Mizuno and Nakamichi 2005). Wild-type alleles of *PPD1 (PPD-1b)* have a rhythmic diurnal pattern of rather low gene expression and are associated with daylength sensitivity (Figs. 11.1 and 11.3). Non-wild-type alleles of *PPD1 (PPD-1a)* alter the expression of the gene, leading to elevated transcription throughout the day, and accelerated flowering through elevated *FT1* expression (Kitagawa et al. 2012). This can substitute for long days and reduce daylength sensitivity.

Several non-wild-type, photoperiod-insensitive alleles are known for *PPD1*. At the *PPD-D1* locus, a 2 kb deletion upstream of the coding

region of the gene confers photoperiod insensitivity of semi-dominant type (Beales et al. 2007). This mutation has been recognized as the major source of earliness in wheat varieties worldwide. Tanio and Kato (2007) described a *PPD-B1a* mutation from the Japanese cultivar FUKUWASEKOMUGI and Nishida et al. (2013) characterized a *Ppd-B1a* allele (a 308 bp insertion in the 5'-upstream region) derived from the Japanese landrace "SHIROBOR21". No genetic locus for *PPD-A1* has been defined in hexaploid wheat. However, Wilhelm et al. (2009) described two photoperiod-insensitive alleles from tetraploid wheat: "*GS-100*" *PPD-A1a* and "*GS-105*" *PPD-A1a*. These alleles have deletions of 1027 bp ("*GS-100*") and 1117 bp ("*GS-105*") in a similar region of the upstream promoter to *PPD-D1a*.

Nishida et al. (2013) described a *PPD-A1a* mutation (1085 bp deletion in the 5'-upstream region) in the Japanese hexaploid wheat cultivar CHIHOKUKOMOGI which is in a similar location to the deletions described by Wilhelm et al. (2009) but appears to be unique to Japanese wheat. In addition to photoperiod-insensitive mutations, Beales et al. (2007) identified candidate null alleles for *PPD-A1* and *PPD-D1* in photoperiod-sensitive cultivars. The loss of function alleles delays flowering time associated with reduced expression of *FT1*, similar to the wild-type alleles (Shaw et al. 2013).

Similar to *VRN1*, there is also variation among the potencies of the three *PPD-1a* loci, where plants with *PPD-A1a* and *PPD-D1a* are earlier in flowering than plants with *PPD-B1a.* Díaz et al. (2012) and Würschum et al. (2015) showed that alleles of *PPD-B1* were associated with increased copy number resulting in earlier flowering. These results, along with multiple copies of *VRN1*, confirm that copy-number variation is important for the adaptation of wheat.

More recently, three candidate genes for *PPD2* and *PPD3* (also designated as *FT3-B1*, *FT3-D1*, and *TOE-B1*) controlling short-day flowering pathway were identified on the long arm of chromosome group 1 in wheat (Zikhali et al. 2014, 2017; Halliwell et al. 2016). Four variations were observed for *FT3-B1* including the wild-type allele, a complete deletion of the gene, a SNP in the exon 3 causing an amino acid change (Gly → Ser), and copy-number variants. Both the deleted and mutated alleles confer delayed flowering under short-day photoperiod (Figs. 11.1 and 11.3). At the *FT3-D1* locus, a SNP in exon 4 was identified. The candidate gene for *PPD3*, *TOE-B1* is still speculative. SNPs in exons 1 and 9 of the *TOE1-B1* gene were shown to separate earlier flowering from later flowering cultivars suggesting the gene to be a putative flowering time repressor, while the mutant allele is expected to attribute earliness (Zikhali et al. 2017). A summary of the role of each gene on the different environmental signals on floral meristem development is again summarized in Fig. 11.4.

11.2.4 Earliness Per Se (EPS) Genes

The photoperiod and vernalization gene systems allow the coarse tuning of adaptation. However, there are still relatively minor variations in flowering time once requirements of vernalization and photoperiod are totally satisfied. These differences are regulated by earliness per se (*EPS*) genes, usually of small effect but critical for fine-tuning developmental phases in the crop cycle (Zikhali and Griffiths 2015; Griffiths et al. 2009). The genetics of *EPS* is still not well understood, and underlying genes with causal polymorphisms have only recently been identified in hexaploid wheat (Zikhali et al. 2017). In wild species *Triticum monococcum* L., a cereal ortholog of *Arabidopsis thaliana* circadian clock regulator *LUX ARRHYTHMO/PHYTOCLOCK 1 (LUX/PCL1)* was proposed as a promising candidate gene for the earliness per se 3 (*Eps-3A*^{m}) locus and the ortholog circadian clock regulator *EARLY FLOWERING 3* (*ELF3*) was identified as a candidate gene for the earliness per se *Eps-A*^{m}*1* locus (Gawroński et al. 2014; Alvarez et al. 2016). *ELF3* was suggested to be the best candidate gene within the *EPS-D1* locus in hexaploid wheat as a deletion containing *ELF3* is associated with advanced flowering (Zikhali et al. 2016). Recently, two

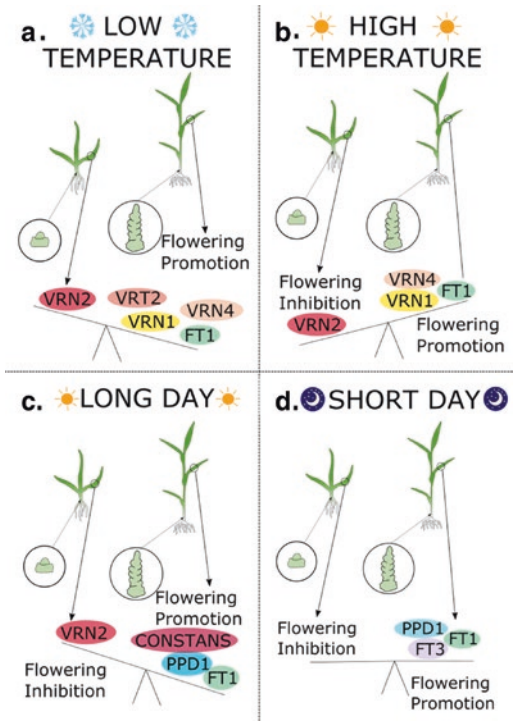

Fig. 11.4 Summary of the roles of different environmental signals on floral meristem development. Different environmental signals are used by plants to regulate the timing and rate of floral meristem development. The relative proportions of the expressed genes are shown in the seesaw summary figures, and the impact of these expression patterns on the floral developmental stage is indicated by the tipping of the seesaw balance. Environmental conditions which are considered are **a** low temperatures, **b** high temperatures (post or non-requiring vernalization), **c** long day, and **d** short day

additional *EPS* QTL in hexaploid wheat located on chromosomes 2B and 7D with the designated names *EPS-B2* and *EPS-D7* were identified (Basavaraddi et al. 2021a), and for the first time, interaction between both genes could be shown. *EPS* genes owe their name to the assumption that they act independent of environment. Despite this, Eps × temperature interaction was recently proven in some instances (Ochagavía et al. 2019; Prieto et al. 2020; Basavaraddi et al. 2021b). In barley, the *EPS* gene *ELF3* has been shown to play a role in the response of circadian clock genes to temperature (Ford et al. 2016).

11.3 Quantitative Trait Loci (QTL) for Flowering Time

The selection of spring and photoperiod-insensitive type cultivars during the evolutionary and breeding history of wheat preceded any methods for gene identification. However, the identification of the causal genes in the last two decades was important to enable targeted selection and therefore the potential for the directed development of new cultivars. One of the major methods utilized in the process of genetic mapping and gene identification is quantitative trait loci (QTL) analysis. QTL analysis is a powerful statistical tool used to calculate the probability of any marker within a genetic map contributing to the observed phenotype. The resolution and reliability of this method is increased via larger mapping populations, as these support higher levels of recombination. The resolution is also increased through an even distribution of markers in the genetic map; however, this is dependent on polymorphisms between the parent genotypes and can be severely limited when diversity is low. This is regularly observed for the D-genome of wheat or when mapping populations are generated between cultivars with a recent shared pedigree. Individual QTL analysis to identify flowering time genes has been conducted for a vast number of mapping populations under a large and diverse set of environmental conditions (for details refer to the next section). These have identified certain genetic hot spots for flowering time regulation, including the regions of major genes previously mentioned, e.g., on chromosomes 5A (*VRN-A1*) along with 7B (*VRN-B3*) and 2D (*PPD-D1*). Within these hot spot regions, it is apparent that multiple genes which regulate flowering time are closely genetically associated. The indication of these genetic hubs, combined with the dominance of the *PPD1* and *VRN1* genes in flowering regulation, suggests that there could be value in assessing the identified QTL for flowering through a meta-QTL (MQTL) analysis. This analysis would identify the number and

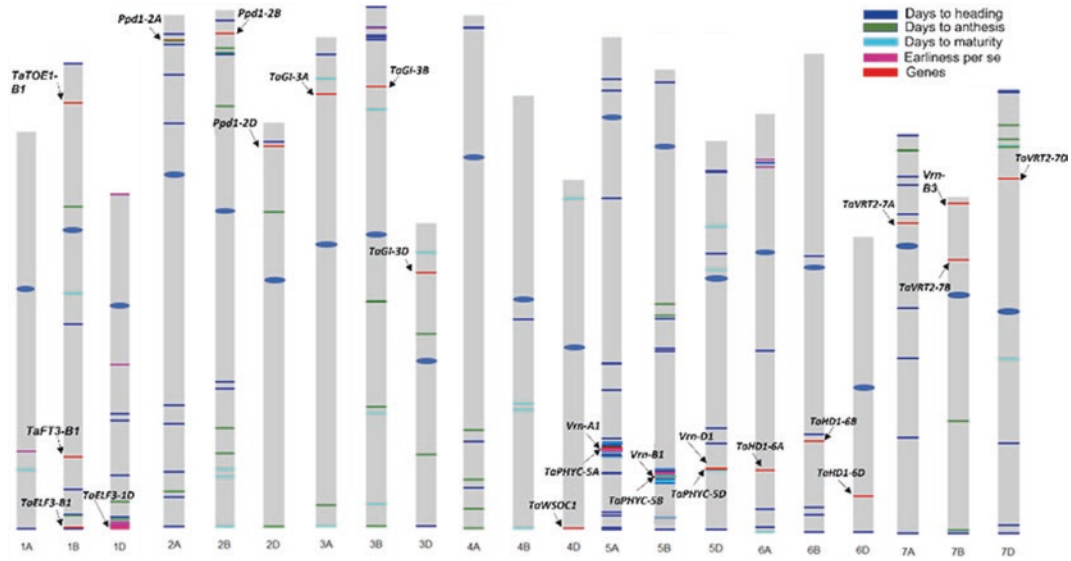

Fig. 11.5 QTL for flowering time-related traits and known major genes projected on the IWGSC RefSeq v1.0. The QTL are shown from short arm (top) to long arm (bottom). Centromeres are presented by blue ovals

genetic range of QTL beyond *PPD1* and *VRN1* and in combination with location information infer some climate-based associations for these additional QTL.

11.3.1 Meta-QTL (MQTL) Analysis

The results of a total of 18 QTL analyses and genome-wide association studies (GWAS) conducted on flowering time in bread wheat were utilized and aligned to the IWGSC-CHINESE SPRING reference sequence (IWGSC RefSeq v1.0) to identify genetic hot spots or MQTL. The studies consisted of 17 mapping populations and five GWAS panels. The traits included were days to heading, days to anthesis, days to maturity, and earliness per se (Supplementary Table S11.1). In addition, 24 flowering genes with known physical locations were integrated (Supplementary Table S11.2). We projected 201 flowering time QTL with 120, 27, 25, and 29 QTL related to days to heading, anthesis, maturity, and earliness per se, respectively (Fig. 11.5). QTL were projected on all chromosomes. The number of projected QTL per genome was 95 (47.3%), 71 (35.3%), and 59 (29.4%) for A, B, and D genomes, respectively. The number of QTL per chromosome ranged from 3 QTL on chromosome 1A to 50 QTL on chromosome 5A.

A window size of 30 Mb was used to infer MQTL. Seven MQTL for flowering time were detected that ranged from 10.5 Mb to 28.7 Mb across chromosomes (Table 11.1). On chromosome 1D, a MQTL1 was identified between 477.9 and 495.1 Mb (MQTL1) and has a size of 17.2 Mb. MQTL2 was located on chromosome 2A between the physical positions of 28.2–43.2 Mb and with a size of 15.0 Mb. On chromosome 2B, MQTL3 was located between 33.9 and 62.6 Mb and has the largest size of 28.7 Mb. MQTL4 was located between physical positions of 30.8–49.0 Mb on chromosome 3B. MQTL5 and MQTL6 were detected on chromosomes 5A and 5B with sizes of 13.8 and 15.1 Mb, respectively. MQTL5 had the maximum number of QTL (36) followed by MQTL6 (14). The MQTL7 was located on chromosome 6A between the physical positions of 67.0–77.5 Mb and had a size of 10.5 Mb.

The MQTL provides the advantage of readily separating QTL which are environmentally more stable, so might have relevance in many

Table 11.1 Summary of flowering time meta-QTL positioned on wheat reference genome IWGSC RefSeq v1.0

MQTL	Chromosome	Range of reference genome V 1.0 (Mb)	Size (Mb)	Number of QTL	Candidate gene
MQTL1	1D	477.9–495.1	17.2	7	*TaELF3-1D*
MQTL2	2A	28.2–43.2	15.0	3	*Ppd1-2A*
MQTL3	2B	33.9–62.6	28.7	3	*Ppd1-2B*
MQTL4	3B	30.8–49.0	18.2	4	
MQTL5	5A	581.1–594.9	13.8	36	*TaPHYC-5A, Vrn-A1*
MQTL6	5B	571.1–586.3	15.1	14	*TaPHYC-5B, Vrn-B1*
MQTL7	6A	67.0–77.5	10.5	4	

different locations globally from those which infrequently occur in QTL analyses. Using this distinction, marker and candidate gene identification can be targeted for specific environmental conditions and so enable the development of a deeper understanding and application of flowering time regulation.

The most frequently identified QTL identified in the MQTL analysis were located on chromosome 5 (A and B genomes) and associated with the *VRN1* region, along with the closely associated *PHYC* gene. A third very robust QTL region was identified on chromosome 1D, overlapping with the *EARLY FLOWERING 3* (*ELF3*) gene, and containing 7 QTL. Additionally, two regions were identified on chromosomes 3B and 6A where QTL were detected in multiple analyses and do not yet have a gene associated with them. Both chromosome regions on 3B and 6A are interesting targets for further investigation. Several QTL were further identified in, potentially, homoeologous regions. These may indicate that the same gene on homoeologous chromosomes contributes to the regulation on flowering time and, therefore, may represent a stable locus but with dosage effect, commonly seen in wheat. Examples for these QTL are in the proximal region of chromosome 5 and the distal region on chromosomes 5, 6, and 7.

11.4 The Effect of Major Genes on the Response to Vernalization and Photoperiod to Developmental Phases and Traits

As an essential trait, the mistiming of flowering can ultimately lead to partial or complete crop failure. However, the focus on time to flowering has meant that additional pleiotropic effects are also selected for, some of which are beneficial. The dominant regulator of vernalization, *VRN1*, is an important gene for the control of the vernalization response and also for the formation of the flower itself, highlighted by its homology to the Arabidopsis *AP1* gene (Yan et al. 2003). *VRN1*, in combination with its homologues *FUL2* and *FUL3*, contribute to the regulation of spikelet formation, plant height, and tiller progression (Li et al. 2019). Furthermore, the regulatory roles of *VRN1* are not limited to floral regulation. The growth of spring vs. winter near-isogenic lines for *VRN1* in barley identified that other traits including root density at specific soil depths were affected (Voss-Fels et al. 2018). In spring barley near-isogenic lines (NILs), root density during grain filling was increased at soil depths between 20 and 60 cm, compared to winter NILs (Voss-Fels et al. 2018).

Like *VRN1*, the regulator of photoperiod response, *PPD1*, is also linked to a number of additional phenotypes. Some of these are closely related to flowering time, for example, the rate of spikelet initiation is accelerated in *PPD1*-insensitive NILs, leading to a reduction in the number of spikelets per spike (Ochagavía et al. 2018). Likewise, the formation of additional or paired spikelets is also altered depending on the *PPD1* allele, a mechanism which is believed to be regulated through the strength of the *FT1* signal (Boden et al. 2015). Beyond the spike architecture, *PPD1* influences grain filling and dry mass production. In durum wheat (*Triticum turgidum* L. var *durum*), cultivars carrying *PPD1* alleles which conferred photoperiod insensitivity allowed earlier flowering and more robust grain filling, leading to enhanced yields. This correlation of effects may not be due to a direct effect of *PPD1* regulating these processes, but might be due to *PPD1* enabling optimal timing of flowering for the particular environment (Royo et al. 2016, 2018; Arjona et al. 2020).

Both the photoperiod and vernalization pathways are integrated through the cereal *FT1-like* gene. As such, allelic variation of *FT1* unsurprisingly shows variation in spikelet number, potentially linked with spikelet initiation rate. The link with spikelet initiation is supported as transgenic lines over-expressing *TaFT1* rapidly flower, while still on the callose regeneration media and produce a spike with only a few, infertile spikelets (Lv et al. 2014). In addition to *FT1*, cereals contain a vastly expanded family of *FT-like* genes, which are becoming a focus for characterization (Bennett and Dixon 2021). *FT2* has been linked with spikelet initiation (Gauley and Boden 2021), while *HvFT3* has also been associated with spikelet initiation in spring lines, independent of a photoperiod signal (Mulki et al. 2018). Interestingly, while *FT3* showed a role in photoperiod-independent spikelet initiation, plants were unable to complete floral development under short-day conditions, indicating that *FT3* alone cannot promote floral development (Mulki et al. 2018). Yet, in winter barley, over-expression of *FT3* could trigger the expression of *HvVRN1* and enable floral development in non-vernalized plants (Mulki et al. 2018). In contrast to this, *FT4* has been identified to function as a repressor of spikelet initiation in barley, with over-expression of *HvFT4* leading to a reduction in spikelet primordia and ultimately grains per spike (Pieper et al. 2021).

11.5 Extending Genetics to Prediction

Flowering time is a critical consideration in the adaptation of wheat to scenarios of changing environments. Future adaptation of any crop in their major producing countries must be forecast because of the substantial time lag in the planning, breeding, and release of new cultivars which can take between 6 and 10 years (Tanaka et al. 2015; Hammer et al. 2020). The delivery of climate-smart solutions for cultivars to be released in a time-reduced and cost-effective manner is a daunting challenge for current agricultural research (Ramirez-Villegas et al. 2020). Based on diverse climate change models, wheat yields will suffer climate change-related declines below current production rates in most regions, with the most negative impact projected to affect developing countries in warmer regions (Pequeno et al. 2021). For example, in a modeling study by Asseng et al. (2015), a decrease in wheat yield gain, namely a fall of 6% yield for each 1 ℃ rise in temperature was predicted, with resultant uncertainty in production over space and time. More recently, Demirhan (2020) estimated a 90.4 million ton drop in global wheat production with a 1 ℃ warming of surface temperature, but a 32.2 million ton increase in production associated with 1 ppm increase in CO_2 emissions. This emphasizes the complexity of climate change and its relationship with vital processes in nature.

To mitigate future uncertainties and to reduce the negative environmental impacts, exploratory simulation models or so-called "adaptation pathways" can be developed (Tanaka et al. 2015). Optimum flowering periods, defined by maximum grain yield potential, are explored by simulating interactions of genotype × environment × management (G × E × M) under current

and future climates for major crops including wheat (Pequeno et al. 2021; Zheng et al. 2012; Flohr et al. 2017; Chen et al. 2020). Thus, statistical and mechanistic models that enable prediction of the performance of plants cultivated in various environmental conditions will play a crucial role in breeding for environmental adaptability and optimization of crop management.

11.5.1 Finding Conceptional Ideotypes for Given Environments

Diagnostic molecular markers associated with the important regulatory genes and QTL related to wheat adaptation (as summarized above) provide a method for identifying existing allelic variation and estimating the effects of each of the alleles in a diverse target production environment. The estimated allele effects can be used to conceptualize ideotypes or genotypes that fit to a specific flowering time range or can predict outcomes of specific crosses in breeding.

Allelic variation in vernalization genes does not contribute to large differences in flowering time in environments where vernalization saturation occurs. A large worldwide panel of varieties was evaluated by Würschum et al. and revealed that a three-component system facilitated the adoption of heading date in winter wheat (Würschum et al. 2018). The *PPD-D1* locus was found to account for almost half of the genetic variance (the photoperiod-insensitive allele *PPD-D1a* mainly present in eastern and southern Europeans as well as in Eurasian cultivars), followed by copy-number variation at *PPD-B1*. Further fine-tuning to local climatic conditions was attributed to small-effect QTL. Sheehan and Bentley (2020) recently documented a dialog with UK wheat agronomists, outlining the requirement of greater flexibility of varietal flowering time (preferably earlier flowering genotypes) in UK winter wheat to find ideotypes for expected changing seasonal conditions, and increasing seasonal weather fluctuations.

In spring wheat, Cane et al. (2013) attempted to define a conceptual genotype or ideotype for environments in southern Australia characterized by variable rainfall in late autumn and early winter. The authors suggested a spring cultivar with slowed development from early sowing, followed by rapid development with increasing temperature and daylength, was an optimal type. The authors defined the allele combination (1) *PPD-B1* (3-copy variant) + *PPD-D1a* + *VRN-A1w* (WICHITA allele) + *VRN-B1* + *VRN-D1a* or (2) *PPD-B1* (3-copy variant) + *PPD-D1b* + *VRN-A1w* (WICHITA allele) + *VRN-B1* + *VRN-D1a* as most suitable. Overall, the variability present in modern Australian spring wheat cultivars was high and diverse combinations of alleles had been successful in the past and were widely grown (Eagles et al. 2009). Recently, Christy et al. (2020) developed a photoperiod-corrected thermal model that solely utilized the combination of *PPD* and *VRN* alleles to predict wheat phenology to identify the phenological suitability of germplasm across the cropping region in southern Australia. Similar to Cane et al. (2013), the authors used their model to identify the optimum allelic combinations required to target optimum flowering period for different locations when sown on different dates. By comparing a series of NILs with different major allele combinations and diverse phenology in the field, Bloomfield et al. (2019) however revealed that a model parameterized solely using multi-locus genotypes is not accurate enough to predict the adoption to flowering time under field conditions. For more accurate predictions, the authors suggested quantifying minor genetic drivers and including genotype × environment (G × E) interaction into models based on genetically derived parameter estimates.

In breeding programs, the major *VRN* and *PPD* loci are usually quickly fixed when targeted at a specific selection environment. In widely adapted CIMMYT spring bread wheat, bred mainly in Mexico but globally distributed through international nurseries and yield trials, the two spring alleles *VRN-B1a*, *VRN-D1a* and the *PPD-D1a*-insensitive allele are the most frequent (Van Beem et al. 2005; Dreisigacker et al. 2021a, b). Also apparent is a strong selection pressure against the spring allele, *VRN-A1a*,

which results in a strong negative effect on the accumulation of biomass and yield at the CIMMYT main selection site at CENEB, in North Mexico, suggesting that genotypes with some vernalization sensitivity are better adapted. Greater allelic variation was found at the *PPD-A1*, *PPD-B1* (including copy number variants), and *VRN-D3* loci. Further, alleles at the two more recently identified photoperiod genes, *TaTOE-B1* and *TaFT-B3*, positively promoted harvest index and yield (Dreisigacker et al. 2021a, b).

11.5.2 Genomic Prediction

With the swift development of next-generation sequencing technologies, whole-genome marker information is generated for all types of germplasm sets. Instead of using only several major loci, genomic prediction/selection aims to utilize whole-genome marker information to predict plant phenotypes (Meuwissen et al. 2001) and thus also includes minor genetic drivers of a trait. While the approach was initially proposed in animal breeding, studies on genomic prediction have been growing in crops including wheat and have become a practical tool in breeding (de Los Campos et al. 2009; Crossa et al. 2010, 2014; Dreisigacker et al. 2021a, b). Flowering time as an important agronomic trait has been predicted with genome-wide markers in wheat using different training and target populations. Within-environment and within single populations' genomic prediction accuracies for flowering time or heading date, measured as the correlation between genomic estimated breeding values and the observed traits, are in the range of 0.4 and 0.7 in the published literature guided by heritability (Charmet et al. 2014; Zhao et al. 2014; Liu et al. 2020; Haile et al. 2021; Crossa et al. 2016).

Predicting the performance of plant phenotypes across diverse environments is more difficult compared to within-environments because phenotypes of more complex traits are often influenced by G × E interaction. Multi-environment trials (METs) for assessing the G × E interaction are therefore common practice in plant breeding for selecting high-performing, well-adapted lines across environments. Models have been developed that evaluate G × E interaction in genomic prediction. Burgueño et al. (2012) were the first to use marker and pedigree genomic best linear unbiased prediction (GBLUP) models to assess G × E. Jarquín et al. (2014) proposed a reaction norm model where the main and interaction effects of markers and environmental covariates are introduced using highly dimensional random variance–covariance structures of markers and environmental covariables. A marker × environment (M × E) interaction model was proposed by Lopez-Cruz et al. (2015) and decomposed the marker effects into components that are common across environments (stability) and environment-specific deviations (interaction). Genomic prediction models that incorporate G × E or M × E interaction have shown to increase prediction accuracies by 10–40% with respect to within-environment analyses (Dreisigacker et al. 2021a, b; Crossa et al. 2017; Pérez-Rodríguez et al. 2017).

Another way to improve the prediction accuracy of G × E is to introduce secondary traits measured in each environment on both the training and target populations in multi-trait genomic prediction models. Recently, Guo et al. (2020) used days to heading as a fixed effect in a multi-trait model with additional yield components in a panel of USA soft facultative wheat. The multi-trait predictions demonstrated higher predictive accuracy than the single-trait models under a multiple-environmental analysis showing its capacity to predict the performance of a genotype for different target environments. Similarly, Gill et al. (2021) used multi-trait, multi-environment genomic prediction which performed best for all agronomic traits in their study including days to heading. Other studies introduce environmental covariates in genomic prediction models to predict the performance of lines in new environments (Jarquín et al. 2014; Heslot et al. 2014; Malosetti et al. 2016; Ly et al. 2018).

11.5.3 Integrating Crop Modeling with Genome-Based Prediction, Phenomics, and Environments

Modular crop model development approaches (Jones et al. 2001) and the rapid advance of QTL analyses conducted for a vast number of populations under diverse environments have opened up opportunities to integrate these two methods (see Box 11.1). This integration allowed the addition, modification, and maintenance of new components, including more recently gene-based functions into process-based crop models (Hoogenboom et al. 2004; White 2009; Zheng et al. 2013; Chenu et al. 2018; Hammer et al. 2019; Robert et al. 2020; Tardieu et al. 2021; Oliveira et al. 2011; Hu et al. 2021; Boote et al. 2021; Cooper et al. 2021; Potgieter et al. 2021; Cowling et al. 2020; Wallach et al. 2018; Hwang et al. 2017; Yin et al. 2018). The first simple gene-based model was developed by White and Hoogenboom (1996) linking gene information with genotype-specific parameters (GSPs) for a drybean model called BEANGRO (Hoogenboom et al. 2019), where seven genes were used to estimate 19 parameters simulating data for 32 cultivars.

Box 11.1 Crop models simulating flowering time

Most crop models use similar approaches to simulate the crop life cycle, integrating development rate over time, usually assuming a potential development rate driven by temperature and modified by several other factors such as photoperiod, vernalization, and other abiotic stresses that may accelerate or delay crop development (Oliveira et al. 2011). The rate of development used in many crop models is a function of a triangular or trapezoidal shape driven by time (TT), or growing degree days (GDD), that are calculated based on maximum and minimum air temperature. The temperature response for wheat has a base temperaure (below which no development occurs) of approximately 0 ºC, optimal temperature (maximum development rate) of approximately 26 ºC, and a maximum temperature (above which no development occurs) of approximately 34 ºC (Hu et al. 2021; Boote et al. 2021). These air temperature thresholds and calculations could vary depending on the crop model used, as some research articles have shown that base and optimal temperature could change during the wheat life cycle, besides soil mean crown temperature being adjusted by snow depth (Hoogenboom et al. 2004; Boote et al. 2021).

The day length effect on crop development is accounted for by a photoperiod sensitivity factor which results in a daily percent reduction of development rate, below the threshold of 20 hours of daylength. The vernalization effect is computed as a function of a vernalization sensitivity factor, or maximum development rate to reach the threshold number of accumulated vernalization days required for a specific cultivar. Vernalization is also lost when daily maximum temperature is above 30 ºC. Vernalization and photoperiod factors are used to modify accumulation of thermal time from emergence to floral initiation (Hoogenboom et al. 2004; Hu et al. 2021; Boote et al. 2021; Cooper et al. 2021).

The process-based modelling approaches mentioned above have been used to predict development of wheat and many crops with good accuracy across many years, having as input other genotype-specific parameters (GSPs) besides weather, soil, and crop management variables (Potgieter et al. 2021). However, only recently have these models started to incorporate true genetic information to capture differences among cultivars instead of empirical GSPs created and calibrated based on processes and observations from field and laboratory studies (Boote et al. 2021; Cowling et al. 2020) even though the idea and first studies started in the late 1990s (Wallach et al. 2018; Hwang et al. 2017; Yin et al. 2018).

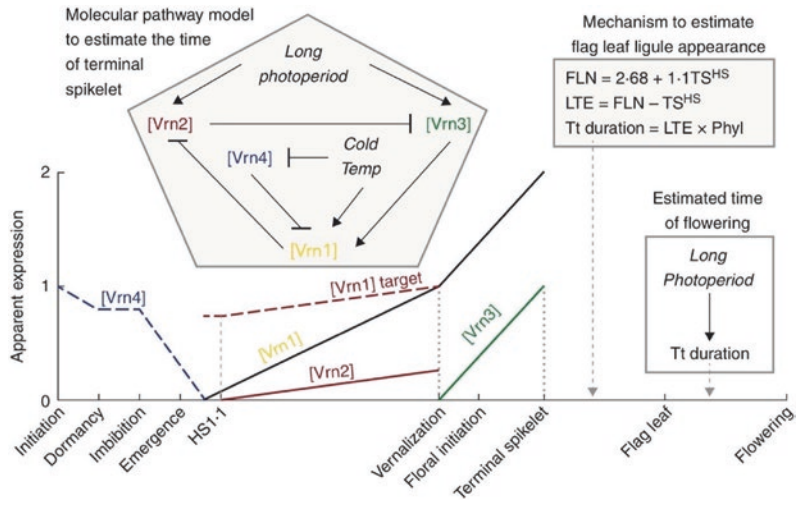

Fig. 11.6 Schematic representation of the integrated model. The crop must pass through each of the phases along the *x*-axis to reach anthesis. Temperature per se controls the progression through each phase in combination with the factors presented. Temperature and photoperiod control the expression of *VRN1*, *VRN2*, *VRN3*, and *VRN4* genes as demonstrated by the scheme within the pentagon (pointed arrows show promotion and flat arrows show repression) and subsequent amount of [Vrn1], [Vrn2], [Vrn3], and [Vrn4] protein expressed as demonstrated by the lines on the graph. The amount of these proteins controls the timing of vernalization and terminal spikelet (adapted from Brown et al. 2013)

Since then, there has been a rapid increase in the number of research studies including gene-based modeling applications, but most of them are still limited to crop phenology and other less complex traits. Brown et al. (2013) integrated molecular and physiological models to simulate time to anthesis using lines of spring and winter wheat under different temperature and photoperiod conditions. They linked the duration of phases to expressions of *VRN* genes to account for the effects of temperature during each developmental stage to develop a model (Fig. 11.6). This analysis framework was compared with CERES, ARCWHEAT1, and SIRIUS model approaches, suggesting the possibility of linking phenological parameters and anthesis time to the alleles or copy number of genes that control the expression of protein signals, relating anthesis genotype to phenotype.

Hu et al. (2021) used the APSIM wheat-G gene-based phenology model to identify the optimal flowering period of spring wheat and concluded that this type of model can identify the best combination of sowing dates and time to flowering to minimize frost and heat risk and achieve higher yields. Among the gene-based modeling applications, those that can be integrated with several other breeding tools have the greatest potential. Wang et al. (2019) reviewed necessary improvements for process-based crop models to simulate $G \times E \times M$ interactions and stated that the verification of temporal gene expression profiles, their environmental dependencies, and their expression levels are further required to trigger key phenological stages.

A growing body of research focuses on the benefits and challenges resulting from the integration of several modern technologies into breeding programs. This includes genomics using dense molecular markers, detailed trait analysis using advances in phenomics, image analyses, and the intense used of environmental covariables (environomics) and multi-trait analysis in order to accelerate genetic gains and

increase agricultural production (Crossa et al. 2019). Incorporating these newly available technologies, e.g., computer simulation for genomic-assisted rapid cycle population improvement, combining rapid genomic cycling with speed breeding, high-throughput phenotyping, and using historical climate and soil data, has potential to improve conventional breeding schemes. Integrating the machinery of crop modeling with that of genomic information and phenomics data together with environomics platforms can further increase the breeding efficiency. This in turn offers great promise to develop varieties rapidly since the selection of candidate individuals can be performed with higher accuracy.

There is evidence that crop models are useful for phenotypic prediction of relevant quantitative traits by simulating the behavior and growth of crops using solar radiation, water, nitrogen, etc., as input. Still, there is little empirical evidence that integration of this type of model with whole-genome prediction increases the prediction accuracy of unobserved cultivars. Two simulation studies (Technow et al. 2015; Messina et al. 2018) showed that integration to a combined model improved prediction accuracy relative to the genomic model alone.

Grain yield is the ultimate measure of crop adaptation due to phenology. Crop models can also be used for prediction of complex traits such as grain yield for different cultivars and location-year combinations within certain eco-geographical regions. It is necessary to incorporate the genetic variance of the traits and how these will change under different environmental conditions into the models. With the rapidly increasing availability of data on DNA sequences of individual cultivars or breeding lines, the use of crop models to improve crop model development and applications has been significantly fast. Similarly, advances in the understanding of the control of plant processes at the molecular level offer opportunities to strengthen how certain plant physiological mechanisms are incorporated into crop models.

It has been shown that crop models can be integrated with genomic prediction to enhance prediction accuracy using simulation data. For example, Heslot et al. (2014) employed crop models to derive stress covariates from daily weather data for predicted crop development stages, by means of the factorial regression model to genomic selection modeling of QTL × environment interaction on a genome-wide scale. The method was tested using a winter wheat dataset, and accuracy in predicting genotype performance in unobserved environments for which weather data were available increased by 11.1% on average. Furthermore, Cooper et al. (2016) used crop models with genomic-enabled prediction applied to an empirical maize drought data set. These authors found positive prediction accuracy for hybrid grain yield in two drought environments.

In general, crop models have been used for crop management decision support. The presence of $G \times E \times M$ interactions for yield presents challenges for the development of prediction technologies for product development by breeding and product placement for different agricultural production systems. Messina et al. (2018) combined simulation and empirical studies to show how to use CGM with genome-enabled methodology for the application to maize breeding and product placement recommendation in the US corn-belt.

In plant breeding, genetic and environmental factors can interact in complex ways giving rise to substantial $G \times E$ interactions that can be used to select genotypes adapted to specific environments. Nevertheless, accurate predictions of future performances in environments are challenging and it requires consideration of the possible weather conditions that may occur within a region and how individual genotypes are expected to react to those conditions. Usually, METs occurring over many years and across multiple locations are utilized to facilitate such predictions. The major challenge is that MET is organized over few years and locations such that genotypes are often advanced without being tested under weather conditions that may critically affect their performance. To overcome this limited scope of the MET, de los Campos et al. (2020) proposed data-driven computer simulations that integrate field trial data, DNA

sequences, and historical weather records for predicting genotype performances and stability using limited years of field testing per genotype.

The data-driven simulation proposed by de los Campos et al. (2020) links modern genomic models that integrate DNA sequences (e.g., single nucleotide polymorphisms—SNPs) and environmental covariates (EC; Jarquín et al. 2014; Crossa et al. 2019) by means of Monte Carlo methods that integrate uncertainty about future weather conditions as well as model parameters (characterized using the their posterior distribution). The importance of this approach is to study ECs as a mechanism to characterize the environmental conditions prevailing during crop growing seasons on the current MET location-year but also in the past field trial data with historical (or simulated) weather records that describe environmental conditions that are likely to occur in a location or region. The results of de los Campos et al. (2020) results show that (1) it is possible to predict the performance of cultivar at environments where these cultivars have few (or none) testing data and (2) predictions that incorporate historical weather records are more robust with respect to year-to-year variation in environmental conditions than the ones that can be derived using only few field trials.

Further research is needed to add evidence that crop modeling together with genomic-enabled predictions can be of benefit in plant breeding together with phenomics and environomics. Three proposed directions for future research are: (a) to use historical data to complement the advantages of crop modeling with those of genomics and phenomics; (b) to conduct more simulation studies with different type of crop models, genomics, and phenomics models and (c) to conduct real experiments where the scientist can control the input of the crop model and measure as accurate as possible the output. Simulation studies should be conducted to benchmark the prediction performance of combined models (crop model + genomics) compared to stand-alone genomic prediction models. Comparing combinations of different types of crop and genomics models, which include random effects for G × E interaction terms, would be useful. New deep learning models that have been developed for dealing with big data sets should also be considered for incorporation with crop models for multi-trait, multi-environment predictions (Montesinos-Lopez et al. 2018, 2019).

11.6 Future Opportunities

Since its first cultivation in 7000 BC, hexaploid wheat has evolved and adapted, enabling expansion underpinning global food security. Adaptive genes (and their complex interactions) have played an important role in optimizing wheat production and will continue to play a significant role in fine-tuning flowering and reproductive cycles suited to changing climates and evolving agricultural production systems. As documented in this chapter, many QTL have been detected with robust effects within and across environments which have expanded the breadth of adaptive variation to be explored in future. However, additional work is required to identify underlying genes and dissect pathways to understand their mode of action and accelerate their validation and deployment in breeding. Likewise, MQTL can help to identify relevant genomic regions over space and time and facilitate the identification of new candidate genes. In the QTL comparison conducted here, we detected seven MQTL regions on chromosomes 1D, 2A, 2B, 3B, 5A, 5B, and 6A. While five MQTL were co-located with known flowering genes regions, candidate genes for two MQTL are not yet known. The identification of genes underpinning the two robust MQTL regions on chromosomes 3B and 6A and those identified to be in homoeologous regions (proximal on 5 and distal on chromosomes 5, 6, and 7) will offer new potential targets for exploitation. These genetic dissection efforts will be greatly aided by current and future developments in wheat genome sequencing and characterization of haplotypes across the wheat and progenitor pangenomes.

Moving beyond the identification of flowering time loci, it will also become increasingly important to understand how genetic regions influence other developmental traits and their responses to environmental factors. This depth of understanding will allow a more targeted "design" of adaptive ideotypes to suit current and future climates and is likely to influence the use of novel breeding methods. For example, the timing of flowering and regulation of distinct flowering stages may influence the efficiency of hybrid wheat seed production, supporting the development of mainstream hybrids. Similarly, genomic selection network approaches that can include multiple traits along with flowering time are likely to be useful in identifying high-performing, optimally adapted lines for breeding, selection, and release. Finally, much future potential exists in applying recently developed integrated genomics and crop modeling approaches. The advances with gene-based modeling in the future, if successful, should make it possible to describe growth and development processes with QTL and other genomic loci analysis, integrated in process-based crop models in a modular approach. This would potentially reduce the need for crop modeling calibration using phenotypic data after new cultivars are released to assess their response to genotype, environment, and management ($G \times E \times M$) conditions. This can both leverage extensive historical data (available in many breeding programs) to identify previously hidden environmental "clues" as well as providing novel targets for the design and deployment of further climate change adaptation strategies.

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