Commentary

When lettuce bolts: natural selection vs artificial selection and beyond

Bolting, the phase transition from vegetative to reproductive development, is a critical step of flowering plants. Determining the timing of bolting is a pivotal life history trait that has evolved over time to optimize reproductive success across diverse environments (Jung & Müller, 2009). In crops like lettuce (*Lactuca sativa* L.), which is primarily cultivated for its edible rosette leaves, bolting marks the end of vegetative leaf production and the onset of flowering (Van Treuren *et al*., 2012). Premature bolting significantly reduces the biomass of vegetative growth in lettuce. Notably, the initiation of flower signaling causes biochemical changes that lead to the accumulation of latex in the leaves, resulting in an undesirable bitter taste and compromising crop quality (Simonne *et al*., 2002). Therefore, unraveling the regulatory networks governing the vegetative–flowering transition would contribute to developing lettuce cultivars resistant to premature bolting. A new paper by Qi *et al*., recently published in *New Phytologist* (2024, doi: 10.1111/nph.20307), identified a key bolting regulator, the LsKN1 (KNOTTED 1) transcription factor, in this process. A natural variation allele of *LsKN1* can modulate the gibberellin (GA) pathway to delay bolting in modern lettuce. This discovery not only advances our understanding of lettuce bolting but also highlights the potential of leveraging natural genetic diversity to improve crop traits and deal with environmental challenges.

> *'Qi* et al.*'s research exemplifies the power of leveraging natural genetic diversity to address key agricultural challenges.'*

The vegetative–flowering transition is regulated by a complex network of genetic and environmental factors. Over the past decade, many genes have been implicated in the control of flowering time in *Arabidopsis thaliana* (Bouché *et al*., 2016). Investigating homologous genes and their regulatory mechanisms has provided insights into the molecular mechanism of bolting in lettuce (Fukuda *et al*., 2011, 2017). However, lettuce has a more complex genome and unique features in terms of vegetable crop traits compared with Arabidopsis. Modern lettuce variants exhibit tremendous morphological variation, especially regarding the rate of transition to flowering (Ryder, 1988; Zhang *et al*., 2017). Genetic variation in lettuce not only serves as a crucial resource for breeding and improvement but also offers opportunities to identify key genes for bolting. In this study, Qi *et al*. generated a segregating population by crossing a crisphead-type cultivar with a stem-type cultivar to map the *LsKN1* allele. They demonstrate that the activated allele, LsKN1^{TP}, resulting from a CACTA-like transposon insertion, delays bolting by reducing GA content through the direct suppression of *LsGA20ox1* expression and the activation of *LsRGA1* expression. Interestingly, LsOFP6 (OVATE family protein 6) functions as a regulatory brake by interacting with LsKN1^{TP}, thereby attenuating its inhibitory effects on GA biosynthesis and signaling responses. This molecular brake mechanism can facilitate environmental adaptability in bolting rates observed in lettuce.

In addition, Qi *et al*. investigated the expression levels of LsRGA1(*REPRESSOR OF GA 1*) across different types of lettuce and revealed lower expression values in stem-type cultivars. This observation raises intriguing questions about how domestication has shaped the genetic architecture of bolting-related traits. Under natural conditions, early bolting may confer adaptive advantages, such as ensuring reproductive success in a vast range of various environments. By contrast, delayed bolting is a trait favored in cultivated lettuce, where prolonged vegetative growth is essential for marketability. This divergence illustrates the evolutionary balance between natural selection in the wild and artificial selection during domestication, suggesting that domestication often results in purifying the selection of genomic regions that control agronomic traits favored by humans.

The discovery of *LsKN1* and its functional role in bolting regulation underscores the importance of exploring genetic variation within lettuce. Wild relative species are often used in crop breeding as a source of novel traits. Lettuce cultivars are domesticated from their progenitor, *Lactuca serriola* (Wei *et al*., 2021), which harbors a wealth of natural genetic diversity, shaped by millennia of evolutionary pressures in diverse environments. *Lactuca serriola* plays a vital role in lettuce breeding, serving as a donor for trait developments, such as carotenoid content, bolting time, water use efficiency, and resistance to diseases and insects (Chadha & Florentine, 2021). Hormonal cross-talk is central to coordinating complex developmental and stress-response pathways. For instance, abscisic acid (ABA) and jasmonic acid (JA), both key regulators of stress responses, often antagonize each other and interact with GA signaling. This raises intriguing questions: can ABA or JA modulate GA-mediated bolting in lettuce? ABA, typically associated with drought responses, might delay bolting by antagonizing GA signaling under water-limited conditions. Similarly, JA, which is implicated in herbivore defense, could intersect with GA pathways to influence resource allocation during bolting. Investigating these interactions in *L. serriola* could uncover

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new regulatory mechanisms, such as how plants balance growth and defense during the vegetative-to-reproductive transition. Understanding these trade-offs could inform strategies to optimize resource allocation in cultivated lettuce.

Additionally, plants of the *Lactuca* genus produce latex, particularly in the stem. This milky fluid, extracted from laticifers, serves as a defense mechanism against herbivores by deterring pests with its bitter taste and sticky texture. More importantly, the latex contains natural rubber (*cis*-1,4-polyisoprene), an important plant derived bioproduct essential in the manufacture of over 40 000 products (Mooibroek & Cornish, 2000). *Lactuca serriola* shows a stronger ability to produce rubber than cultivated lettuce, along with a higher biomass yield (Bushman *et al*., 2006). It is also tolerant and well adapted to cultivation on marginal land, alleviating field competition with food crops. As such, it has great potential to be a new type of crop after *de novo* domestication (Li *et al*., 2018) for producing high-quality natural rubber. The fact that the synthesis of rubber takes a lot of energy out of the plant is another mystery. Considering that it cannot be metabolized, what value does it have to the plant? It has been suggested that rubber is produced in the plant as a response to its overproduction of photosynthesis and is therefore likely to be a metabolic 'spillover' (Paterson-Jones *et al*., 1990). Moreover, it has been reported that the initiation of flower signaling leads to the accumulation of latex. Is there a potential link between bolting and latex production? Could there be an energy metabolism trade-off, or is there a more efficient mechanism for energy allocation? Investigating this question from an evolutionary standpoint may offer deeper insights into the molecular mechanisms governing bolting in lettuce. Elucidation of this intriguing phenomenon not only deepens our understanding of bolting regulation in lettuce but can also facilitate the *de novo* domestication of wild lettuce to produce natural rubber.

Qi *et al*.'s research exemplifies the power of leveraging natural genetic diversity to address key agricultural challenges. By identifying *LsKN1* as a master regulator of bolting and linking its activity to hormonal signaling pathways, their study advances our understanding of lettuce development and provides actionable insights for breeding programs. Wild relatives like *L. serriola* are more than genetic resources for improving agronomic traits, they are living repositories of evolutionary adaptations. Traits, such as stress resilience and latex production, offer valuable lessons for enhancing plant productivity and defense. At the same time, the crosstalk between hormonal pathways like GA, ABA, and JA highlights the intricate regulatory networks that underpin plant development and survival. Preserving and studying wild lettuce populations is crucial for unlocking their full potential. As global agriculture faces mounting pressures from climate change and resource scarcity, *L. serriola* serves as a reminder of the untapped solutions inherent in nature's diversity. By integrating insights from wild and domesticated populations, researchers can bridge the gap between fundamental plant biology and applied agricultural innovation, ensuring a sustainable future for crop breeding.

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