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The arches and spandrels of maize domestication, adaptation, and improvement

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Abstract

People living in the Balsas River basin in southwest México domesticated maize from the bushy grass teosinte. Nine thousand years later, in 2021, Ms. Deb Haaland — a member of the Pueblo of Laguna tribe of New Mexico — wore a dress adorned with a cornstalk when she was sworn in as the Secretary of Interior of the United States of America. This choice of garment highlights the importance of the coevolution of maize and the farmers who, through careful selection over thousands of years, domesticated maize and adapted the physiology and shoot architecture of maize to fit local environments and growth habits. Some traits such as tillering were directly selected on (arches), and others such as tassel size are the by-products (spandrels) of maize evolution. Here, we review current knowledge of the underlying cellular, developmental, physiological, and metabolic processes that were selected by farmers and breeders, which have positioned maize as a top global staple crop.

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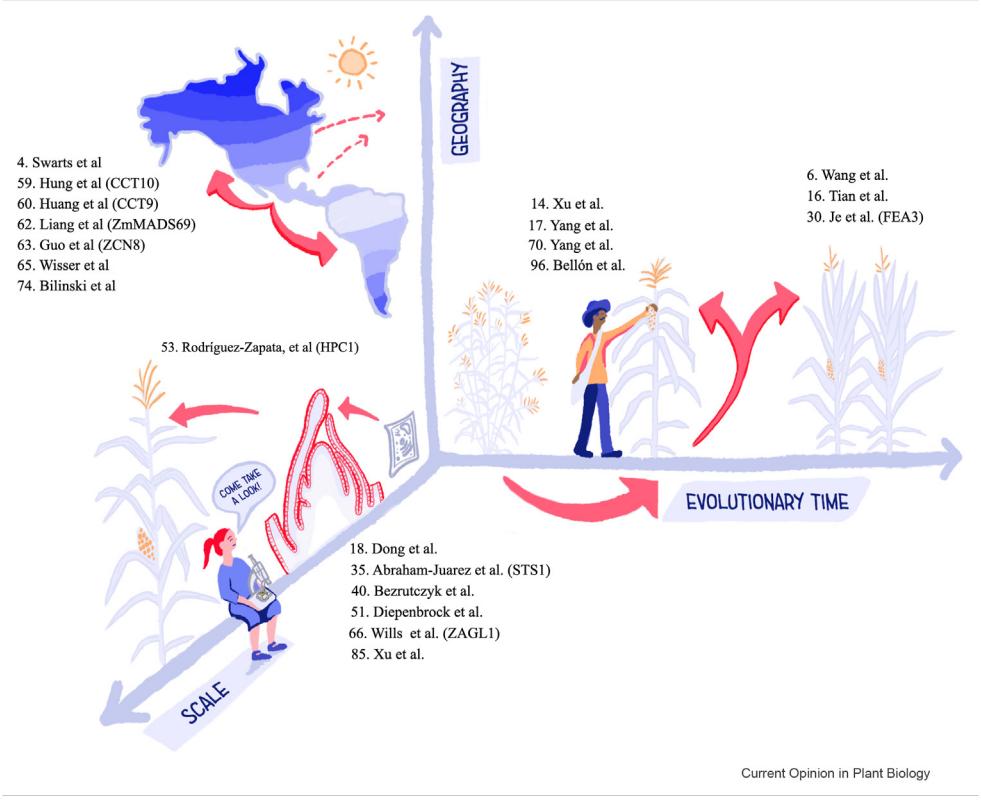
The domestication of maize from teosinte (Figure 1) [1,2], as well as its expansion to new environments, local adaptation [3–5], and genetic improvement [6,7], reduced overall genetic diversity through selection and bottlenecks. Teosinte is a key resource for identifying loci that regulate architectural traits that have been lost during domestication, because maize shoot morphology has a considerable impact on yield-related traits, such as plant density and inflorescence and kernel production [8–10]. Recently, several quantitative trait loci (QTL) and candidate alleles related to the evolution of maize shoot architecture were mapped using maize-teosinte recombinant inbred line populations [11–17]. Using this approach, Tian et al. identified *UPA1* (*Upright Plant Architecture 1*) and *UPA2*, two major QTL for upright plant architecture. *UPA2* is a *cis*-regulatory variant, whereas *UPA1* encodes a biosynthesis enzyme for the phytohormone brassinosteroid [16]. Introgression of the teosinte allele of *UPA2*, which promotes more upright blades, into maize hybrid lines permitted denser planting and enhanced grain yield [16]. Although this study demonstrates the importance of wild relative alleles on shoot architecture and yield, the average selection intensity for reproductive traits was found to be double that for vegetative traits, highlighting the importance of altering ear morphology [17].

Reduced axillary branching is a common trait in many domesticated crop plants compared with their wild ancestors [18], and modifications of these developmental patterns are fine-tuned at the regulatory level by dynamic interactions between proteins, transcription factors, and noncoding elements [19]. In maize, increased apical dominance was key for domestication, and it was achieved by the gain of function of the transcription factor *tb1* (*teosinte branched1*). Tb1 has been proposed as a crucial negative regulator of cell growth that modulates several domestication genes, including *gt1 (grassy tillers1)*, *tru1 (tassels replace uppers ear1)*, and *tga1 (teosinte glume architecture1)* [18,20]. Indeed, some groups of genes related to crop domestication and improvement have been reported, with maize TCP, bHLH, and MADS families highly represented [21]. As per *tb1* function, mutant *tb1*, *gt1*, and *tru1* plants overproduce tillers and aerial branches owing to altered bud dormancy [22–24].

Figure 1



Axes of maize selection. Three axes on which human selection has acted on during maize domestication, adaptation, and improvement and some of the traits that have been the results of this selection. The Y-axis represents the environmental and geographic changes that maize had to adapt after domestication in current Mexico. Coloring in the map of America indicates day length. The X-axis indicates how selection by farmers and breeders has acted to change whole plant architecture such as tillering, ear height, tassel size, and so on. The z-axis shows how changes at the metabolic, physiological, genomic, and cellular levels underlie whole plant architecture changes. References indicate some of the key studies and genes involved in processes in each of the three axes.

Furthermore, TB1 targets phytohormones and sugars by positively regulating abscisic acid and jasmonic acid and negatively regulating gibberellin and the sucrose transporter *SWEET15b* [18].

RNA-seq and ChIP-seq experiments have contributed to a better understanding of the regulatory network controlled by TB1 and GT1, explaining how allelic variation in this transcriptional hub produced drastic architectural changes that were agronomically beneficial. Among TB1 targets were genes related to light perception and response to red and far-red light [18]. This observation fits the previously described function of *tb1*, where *PHYTOCHROMEB* perceives shading as a low red/far-red light ratio and initiates a signaling cascade promoting *TB1* and *GT1* suppression of lateral bud outgrowth in the shade [18,23]. In domesticated maize, the *TB1-GT1* module conditions constitutive repression on axillary bud growth, which is perceived as insensitivity to shade avoidance response, a distinctive trait compared with teosinte [23,25]. Selection for bud growth repression together with selection for upright leaf angles has contributed to the increase of plant densities in modern breeding [6], a fundamental factor of increased yields per surface area [26].

Plant architecture depends on the activity of shoot apical meristems (SAMs) (Figure 1) [27]. The CLV-WUS (CLAVATA-WUSCHEL) module is a key feedback pathway that regulates communication between cells within the SAM in different plant species [28]; in maize, CLV orthologs, FEA (FASCIATED EAR) receptor-like proteins, and WUS proteins have been studied primarily in the inflorescences [29,30]. In this same pathway, ZmCRN (CORYNE), a signaling protein, functions downstream of FEA2/CLV2, which transmits signals from CLE (CLV3/ESR-RELATED) peptides through interactions with CT2 (COMPACT PLANT2) and ZmCRN [31]. Interestingly, other FEA proteins have been identified functioning in parallel pathways to CLV-WUS, for example, FEA4 promotes differentiation in the SAM periphery in opposition to

KN1 (KNOTTED1) and WUS [32]. These pathways illustrate how cell−cell communication through signal transduction pathways fine-tunes inflorescence meristem activity, a target in maize domestication in search of larger ear meristems. Recently, it was reported that use of CRISPR-Cas9 genome editing to make weak promoter alleles of maize *CLE* genes increased multiple grain yield-related traits, two *ZmCLE7* fragment promoter deletion alleles showed a significant increase in most yield-related traits including weight and grain yield per ear, and some others showed compensation and redundancy of *ZmCLE7* null alleles [33]. Showing that in the genome editing era, rapid domestication can be achieved more efficiently. Furthermore, recreation of ancestral proteins in maize into novel versions that harbor small changes in sequences, either by genome editing or transgenesis, highlights the potential for inducing gradual evolution in plant morphology [34,35].

Advances in plant single-cell and single nucleus 'omics' are forging new opportunities to overcome organ and tissue heterogeneity [36]. Single-cell transcriptomic studies in maize highlight previously unappreciated developmental and physiological changes in germinal cells [37]. Vegetative and reproductive meristems historically have been recalcitrant to isolating viable protoplasts (plant cells without their cell wall). Recent reports in the maize shoot apex and developing ear have cleared technical hurdles for obtaining thousands of protoplasts from shoot meristems for single-cell transcriptomics [38,39]. In more differentiated maize leaf tissues, scRNA: single cell RNA sequencing (scRNA-seq) uncovered novel transcript accumulation of *SWEET13* paralogs in abaxial bundle sheath cells that surround rank-2 veins [40]. Furthermore, individualizing nuclei and assaying accessible chromatin by sequencing identified cell-specific lineages by enrichment of accessible chromatin regions (ACRs), which often have transcription factor DNA-binding motifs in proximity to genes with cell-specific expression [41]. Moreover, physical interactions between distal ACRs and genes, especially for agronomically important loci, that were found previously in whole tissues [42] were also detected in single nuclei [41]. ACRs are highly conserved across plant species [43], and single-cell/nucleus applications have the potential to revolutionize comparative studies. For example, by deciphering cell-type-specific transcriptomes or chromatin status between teosinte and domesticated maize and/or by incorporating plants grown in modeled domestication conditions [44], such strategies could lead to understanding how environmental changes affected gene expression in certain cell lineages during domestication.

Humans have selected secondary metabolites that impact color, sweetness, and other kernel traits that are related to flavor and general organoleptic properties [45]. Indeed, genes such as *ZmSWEET4c* involved in sugar transport into the seed show signals of selection in domesticated maize (and rice) when compared with teosinte [46]. Vallebueno et al. [47] suggest that the timing of selection on *TB1* may point out that domestication could first be targeted to increase stalk biomass for direct consumption. Later on, sweet corn was developed by indigenous people, with mutant *SU1* alleles having been fixed and cultivated three separate times in North America [48]. Selection for a reduction in grain bitterness may have led to a reduction of alkaloids in maize when compared with teosinte [49]. Many of the metabolic changes taking place during domestication were unintended, so to compare them is informative in assessing the nutritional composition and differences between crops and their progenitors. Fang et al. [50] found that there is similar genetic architecture in maize and teosinte oil and carotenoid variation and that maize traits underwent a strong and recent selection during and after domestication. Carotenoids in particular are an area where work is being performed to harness natural variation to increase levels and regain nutritional content for locations where maize is a nutritional staple [51]. A recent study compared the metabolites of a BC2S7 population created by crossing a highland teosinte (*Zea mays* ssp. *Mexicana*) with Mo17, a modern maize inbred line, and showed that long-term domestication and breeding reshaped amino acid metabolism, likely to meet demands in high-yielding modern varieties [52]. The origin of many of the most favorable alleles resulting in altered sugars, amino acids, or tricarboxylic acid cycle intermediates came from teosinte [52]. Other favorable metabolic traits introduced from highland teosinte may have helped maize adapt to higher altitudes and lower temperatures. A teosinte introgression into some highland maize landraces carries a favorable allele that alters membrane lipid quantities by increasing the amount of phosphatidylcholine [53]. Several other genes in the phospholipid pathways of maize have shown accelerated evolution to cold, as well [54].

Humans did not just adapt teosinte into modern maize, but they have also adapted and relocated tropical maize into more temperate climates that required additional metabolic changes. Deng et al. [55] found that 39.8% of metabolites analyzed were significantly altered between tropical and temperate maize kernels. The genetic architecture of genes involved in metabolomic differences between temperate maize and tropical maize is simpler (fewer changed genes and larger effect sizes) than maize and its wild relatives, probably reflecting the shorter evolutionary divergence between temperate and tropical maize. Alkaloids, terpenoids, and lipids were targeted when tropical and temperate maize diverged. For example, 2,4-dihydroxy-7-methoxy-1,4-benzoxazin-3-one (DIMBOA) compound concentrations are higher in temperate maize than tropical maize and at least one

such compound, 2,4-dihydroxy-7-methoxy-1,4-benzoxazin-3-one glucoside (DIMBOA-Glc), may be important for local adaptation of temperate maize to resist new insect pressure [49].

Photoperiod adaptation was a key component that enabled maize to expand across the Americas after domestication [4,56] (Fig. 1). This was particularly crucial as it moved northward to the United States where day lengths are longer during the growing season, delaying flowering time in unadapted tropical maize. Photoperiod adaptation was not an issue as maize moved southward, and this may have facilitated the rapid expansion of maize to Central and South America after domestication [57,58]. The nested association panel was used to identify the major QTL involved in photoperiod sensitivity [59]. Major genes that increase photoperiod sensitivity include *ZmCCT (CO-like/COL and TOC1) 9* [60], *ZmCCT10* [61], and *ZmRap2.7* [62]. On the other hand, *ZCN8 (CENTRORADIALIS8),* the most commonly known/studied maize florigen gene, decreases photoperiod sensitivity [63]. Adaptation to temperate latitudes resulted in additive selection of genetic variants that increase the activity of ZCN8 [63] and decrease the activity of ZmCCT9 [60] and ZmCCT10 [64] leading to reduced photoperiod sensitivity. Artificial evolution experiments that selected for shorter flowering of tropical maize populations recapitulated the evolutionary process of tropical maize adaptation and identified the same major key regulators of photoperiod sensitivity [65]. Other genes, such as *zagl1* (zea agamous-like1), that are not necessarily involved in photoperiod sensitivity but can reduce flowering time, were also under strong selection during maize domestication [66]. Genes involved in maize flowering time can also exhibit pleiotropic effects, as observed with *zagl1*'s effect on increased ear size [66] and the effect of a *ZmCCT* gene on resistance to Gibberella stalk rot [67].

Before maize was brought to northern latitudes, it first was adapted to the highlands of México, Central America, and South América. In highland environments, low temperatures that lead to slow heat unit accumulation have imposed a strong selection for early flowering genetic variants and/or against late-flowering variants. Genomic scans of highland adapted materials have identified that flowering time genes are under selection in highland maize [68,69]. Highland teosinte (*Z. mays* ssp. *Mexicana*) is a source of early flowering alleles in highland maize [53]. Introgressed early flowering alleles have been conserved in temperate maize [53,63], pointing to a relevant role of highland teosinte mexicana introgression [70] in maize adaptation to environments where the ability to photosynthesize in low-temperature conditions [71] and flower early is advantageous. Teosinte *mexicana* is found in the Mesomerica highlands but not in South America. However, evidence shows significant gene flow between highland populations of Mesomerica and South America [69], so the role of teosinte *mexicana* derived alleles in South America highland maize adaptation cannot be ruled out. Strong selection for early flowering affects several developmental and genomic traits that enable faster development, growth, and flowering, which contributed to local adaptation. SAM size and flowering time are inversely correlated such that maize with large meristems flowers earlier than maize with small meristems [72,73]. Larger cells and faster leaf cell production rates are also correlated with smaller genome size in maize and teosintes, and in turn, maize and teosintes with smaller genome sizes are more prevalent at high elevations [74,75]. In theory, smaller genome sizes should enable faster cell replication rates and facilitate faster development; indeed, artificial selection experiments have shown that selection for early flowering does indeed reduce genome size [76].

Perspective and outlook

Comparative morphology and genomics will continue to be foundational to future studies on maize domestication and adaptation. The current genomics era is providing a more complete understanding of maize evolution as more high-quality genome assemblies for maize inbred lines [77], landraces [78], and wild relatives [70] become available, in addition to the construction of a pangenome graphical representation of haplotypes [79]. This collective wealth of genomic information, together with the development of new gene-editing technologies in an ever-growing number of genotypes [80,81], is enabling CRISPR/Cas9 high-throughput mutagenesis [82], trait stacking in precise genome locations [83], and even targeted chromosomal inversions [84]. Technologies that leverage this wealth of genomics, such as single-cell/single-nucleus 'omics' [37,38,40,41,85], assays that infer genome-wide DNA binding landscapes and associations between transposons, regulatory regions, and target genes [86–90] and evolutionary-guided machine learning methods to predict levels of gene products [91] will continue to foster and inform innovative strategies to study and modify maize genetic variation, conceivably at precise cell-type or pathway resolution.

The development of more diverse mapping populations with open-pollinated maize landraces [53,65] and wild relatives [92–94] together with genomic scans of selection has proven to be a powerful tool to uncover loci contributing to domestication and local adaptation, and the important roles that teosinte parviglumis [16] and the highland teosinte mexicana have in modern maize [53,63]. The ability to identify domestication- and adaptive-QTL/QTN and QTL by environment interactions will gain further momentum as more maize-teosinte mapping populations are generated and large-scale common garden experiments [68,95] with an ever-growing number of genotypes are implemented.

Finally, we hope that our highlighting the decades of attention to understanding the genetic basis of maize domestication and adaptation is accompanied by an appreciation (Figure 1) of the fundamental roles that smallholder farmers and campesinos have played — and continue to play — in the development and maintenance of maize diversity and, ultimately, in ensuring present and future food security [96].

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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