Review Article

Cucurbitaceae genome evolution, gene function, and molecular breeding

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Abstract

Cucurbitaceae is one of the most genetically diverse plant families in the world. Many of them are important vegetables or medicinal plants and are widely distributed worldwide. The rapid development of sequencing technologies and bioinformatic algorithms has enabled the generation of genome sequences of numerous important Cucurbitaceae species. This has greatly facilitated research on gene identification, genome evolution, genetic variation, and molecular breeding of cucurbit crops. So far, genome sequences of 18 different cucurbit species belonging to tribes Benincaseae, Cucurbitae, Sicoeae, Momordiceae, and Siraitieae have been deciphered. This review summarizes the genome sequence information, evolutionary relationships, and functional genes associated with important agronomic traits (e.g. fruit quality). The progress of molecular breeding in cucurbit crops and prospects for future applications of Cucurbitaceae genome information are also discussed.

Introduction

Cucurbitaceae is the second largest fruit and vegetable family and its members are among the most important edible plants in the world, next only to Solanaceae [1,2]. The family contains ~115 genera and 960 species, which are mostly herbaceous annual vines or perennial lianas, often with tendrils [3]. They can be monoecious or dioecious (occasionally hermaphrodite) and are mainly distributed in tropical and subtropical zones, rarely in temperate zones [3]. A characteristic feature of the Cucurbitaceae is the existence of bicollateral vascular bundles where the phloem is present on both the outer and the inner side of the xylem [4]. Cucurbit species frequently contain cucurbitacin, which is the main substance causing the bitter taste [5]. The family Cucurbitaceae contains a variety of vegetables or fruit crops, which are of great significance to the global or local economy. The vegetables include cucumber (Cucumis sativus), zucchini (Cucurbita pepo), pumpkin (Cucurbita maxima, Cucurbita moschata, and Cucurbita argyrosperma), wax gourd (Benincasa hispida), bottle gourd (Lagenaria siceraria), bitter gourd (Momordica charantia), ridge gourd (Luffa acutangula), sponge gourd (Luffa cylindrica), chayote (Sechium edule), and snake gourd (Trichosanthes anguina), and the fruits include melon (Cucumis melo), horned cucumber (Cucumis metuliferus), watermelon (Citrullus lanatus), and luo-han-guo (Siraitia grosvenorii) [2,3]. Among them, bitter gourd and luo-han-guo both have rich edible and medicinal value [6] and snake gourd and bottle gourd can be used as food and ornaments [7,8].

Recently, thanks to the rapid advances in sequencing technologies and bioinformatic algorithms, the application of whole-genome sequencing technology in biology has become more and more common [9]. Due to the high cost and low throughput of Sanger sequencing, the initial genome sequencing work was limited to few plant species, mainly model species such as Arabidopsis thaliana [10] and Oryza sativa [11]. The first Cucurbitaceae crop genome, that of cucumber, was sequenced using Sanger and next-generation Illumina sequencing technologies and released in 2009 [12]. With the emergence of next-generation sequencing, the cost of sequencing was greatly reduced and efficiency
was substantially improved, making possible whole-genome sequencing of many commercially important plants in addition to model organisms. Most importantly, third-generation sequencing technologies (e.g. Oxford Nanopore and Pacific Biosciences) that produce longer reads instead of short reads, chromosome conformation capture techniques, and novel computational methods have together improved the completeness and contiguity of genome assemblies [13, 14]. To date, a number of Cucurbitaceae genomes have been assembled, including Cucumis sativus [12, 15–19], Cucumis melo [20–25], Cucumis hystrix [26], Cucumis × hystrix [27], Cucumis metuliferus [28], Cucurbita pepo [29], Luffa siceraria [30], C. citrullus lanatus [31–33], Cucurbita moschata, Cucurbita maxima [34], Cucurbita argyrosperma [35, 36], B. hispida [37], Luffa cylindrica [38–40], Luffa acutangula [40], M. charantia [6, 41, 42], Siraitia grosvenorii [43, 44], T. anguina [45], and Sechium edule [46]. The completion of genome sequencing of several Cucurbitaceae crops has injected new impetus into the study of genome structure and functional evolution of Cucurbitaceae. This is of great practical significance for further study of the Cucurbitaceae at the genomic level, understanding biological mechanisms, and improving the quality of Cucurbitaceae crops at the molecular level. This review summarizes the findings of whole-genome sequencing and resequencing of Cucurbitaceae plants, which have provided basic data for genome-wide studies of important Cucurbitaceae plants, and discusses the molecular regulation of important traits and prospects for their application to improving fruit quality and promoting plant breeding.

**Whole-genome sequencing of cucurbit crops**

As sequencing technologies have developed rapidly, the experimental data and genome sequences of some species have been reinterpreted or revised and improved using new technologies, and this has enabled more complete genome assemblies to be constructed [16, 24]. The cucumber genome sequence [12] was quickly followed by melon [23] and watermelon [31] sequences. Many improved or new genome assemblies of Cucurbitaceae species have been produced during the past 5 years (Table 1). The assembled genome sizes of Cucurbitaceae crops range from 204.8 to 919.76 Mb with a scaffold N50 ranging from 620.88 kb to 82.12 Mb.

According to the reported syntenic relationships among genomes of cucurbits, including melon (n = 12), cucumber (n = 7), wax gourd (n = 12), bottle gourd (n = 11), watermelon (n = 11), and pumpkin (n = 20), it is inferred that the ancestral cucurbit protochromosome number was 15 and the most ancestral state is preserved in the wax gourd genomes among these species [37]. Collinearity analysis showed that the seven chromosomes of wax gourd genomes among these species [37]. Collinearly analysis showed that the seven chromosomes of wax gourd genomes among these species [37]. Collinearly analysis showed that the seven chromosomes of wax gourd genomes among these species [37]. Collinearly analysis showed that the seven chromosomes of wax gourd genomes among these species [37]. Collinearly analysis showed that the seven chromosomes of wax gourd genomes among these species [37]. Collinearly analysis showed that the seven chromosomes of wax gourd genomes among these species [37]. Collinearly analysis showed that the seven chromosomes of wax gourd genomes among these species [37]. Collinearly analysis showed that the seven chromosomes of wax gourd genomes among these species [37].

**Genome evolution**

Besides the whole-genome triplication event (gamma) shared by all eudicots, it seems that at least four additional whole-genome duplication (WGD) events occurred during the evolution of Cucurbitaceae plants [2]. An early large-scale duplication event (CucWGD1), a cucurbit-common tetraploidization at the origin of the Cucurbitaceae family, has been identified, which occurred shortly after the gamma event (115–130 Mya) [2, 46, 47]. Moreover, three relatively recent WGDs have been identified within three tribes [2]. The tribe Cucurbitae probably experienced one WGD at its origin (CucWGD2) [34]. Several studies have shown that zucchini (Cucurbita pepo), pumpkin (Cucurbita moschata and Cucurbita maxima), and silver-seed gourd (Cucurbita argyrosperma) from the tribe Cucurbitae underwent WGD events [29, 34, 35]. In addition, several members of the tribe Sicyoeae also exhibit evidence for one WGD event (CucWGD3) [2]. One recent WGD event occurred in chayote (Sechium edule) of the tribe Sicyoeae at about 25 ± 4 Mya [46]. CucWGD4 is likely shared by the members of Hemisleyae in the Gomphogyneae tribe [2].

According to the evolutionary relationship among Cucurbitaceae [26, 28, 30, 34, 37, 39, 42, 44–46], we summarized the phylogeny of 17 sequenced Cucurbitaceae species (Cucumis × hystrix is not included) by integrating relevant information (Fig. 1). Phylogenetic analysis indicates that a variety of fruit and vegetable Cucurbitaceae crops emerged with different shapes due to species
| Date | Sequencing technologies | Cucurbitaceae species | Accession name | Chromosome number (n) | Genome size (Mb) | Contig N50 (kb) | Scaffold N50 (Mb) | Ancestral (Mb) Oriented (Mb) Complete (Mb) | protein-coding genes | Repetitive sequences (%) | BUSCOs (%) |
|------|-------------------------|-----------------------|----------------|----------------------|-----------------|----------------|-----------------|-------------------------|------------------------|-------------------------|----------------|
| 2009 | Singer and Illumina     | Cucumber [12](Cucumis sativus var. sativus) | 7 | 543.50 | 19.80 | 263.00 | 23.80 | 0.32 | 363.30 (87.52%) | 291.90 (80.77%) | 21.90 | 2436 |
| 2011 | 454, Sanger- Celera/Arachne | Cucumber [17](Cucumis sativus var. sativus) | 7 | 323.00 | 23.80 | 648 | 18.20 | 4.68 | 316.30 (87.52%) | 291.90 (80.77%) | 21.90 | 2436 |
| 2012 | 454 | Melon [23](Cucumis melo) | 12 | 375.00 | 18.20 | 648 | 18.20 | 4.68 | 316.30 (87.52%) | 291.90 (80.77%) | 21.90 | 2436 |
| 2013 | Illumina | Cucumber [18](Cucumis sativus var. sativus) | 7 | 193.00 | 139.00 | 23.80 | 648 | 18.20 | 4.68 | 316.30 (87.52%) | 291.90 (80.77%) | 21.90 | 2436 |
| 2016 | Illumina | Melon [22](Cucumis melo) | 11 | 344.00 | 15.00 | 648 | 18.20 | 4.68 | 316.30 (87.52%) | 291.90 (80.77%) | 21.90 | 2436 |
| 2019 | Illumina | Melon [24](Cucumis melo var. inodorus) | 12 | 386.00 | 2860.00 | 380.79 (98.53%) | 363.76 (95.53%) | 92.78 | 49.80 | 22924 |
| 2019 | Illumina | Melon [25](Cucumis melo var. inodorus) | 12 | 386.00 | 2860.00 | 380.79 (98.53%) | 363.76 (95.53%) | 92.78 | 49.80 | 22924 |
| 2019 | Illumina | Melon [26](Cucumis melo var. inodorus) | 12 | 386.00 | 2860.00 | 380.79 (98.53%) | 363.76 (95.53%) | 92.78 | 49.80 | 22924 |

(Continued)
| Date | Sequencing technologies | Cucurbitaceae species | Accession name | Chromosome number (n) | Genome size (Mb) | Contig N50 (kb) | Scaffold N50 (Mb) | Anchored (Mb) | Oriented (Mb) | Complete BUSCOs (%) | Repetitive sequences (%) | Protein-coding genes |
|------|------------------------|----------------------|----------------|----------------------|-----------------|----------------|-----------------|----------------|--------------|----------------------|--------------------------|------------------------|
| 2019 | PacBio, 10X Genomics, and Hi-C technologies | Cucumber [16] (Cucumis sativus var. sativus) | 'Chinese long' inbred line 9930 | 7 | 226.20 | 8900.00 | 11.50 | 211.00 (93.30%) | 36.43 | 24317 | 91.00 | 75.50 | 27467 |
| 2019 | Illumina and PacBio | Waxgourd [37] (Benincasa hispida) | Inbred line B227 | 12 | 913.00 | 68.50 | 3.40 | 859.00 (94.10%) | 91.00 | 36927 | 95.30 | 55.82 | 33829 |
| 2020 | Illumina and PacBio | Cucumber [19] (Cucumis sativus var. sativus) | B10 | 7 | 342.29 | 858.00 | 91.30 | 27271 | 95.30 | 55.82 | 33829 | 95.30 | 55.82 | 33829 |
| 2020 | PacBio | Melon [20] (Cucumis melo) | DHL92 | 12 | 357.64 | 714.00 | 17.50 | 343.00 (96.00%) | 94.80 | 29890 | 95.30 | 55.82 | 33829 |
| 2020 | ONT, Bionano optical map, Illumina HiSeq, mate pair, and linkage map information | Snake gourd [45] (Trichosanthes anguina) | | 11 | 919.76 | 20110.00 | 82.12 | 918.80 (99.89%) | 95.38 | 22874 | 95.38 | 80.03 | 22874 |
| 2020 | Illumina and PacBio | Spongegourd [38] (Luffa cylindrica) | Inbred line P93075 | 13 | 656.19 | 8800.00 | 48.76 | 63.81 | 25508 | 92.70 | 62.18 | 31661 |
| 2020 | SMRT and Chicago/Hi-C | Ridge gourd [39] (Luffa acutangula) | Inbred line AG-4 | 13 | 734.60 | 0.79 | 92.70 | 62.18 | 32323 | 93.00 | 56.78 | 43828 |
| 2020 | SMRT and Chicago/Hi-C | Spongegourd [39] (Luffa cylindrica) | Inbred line SO-3 | 13 | 689.80 | 0.58 | 93.00 | 56.78 | 43828 |
| 2020 | PacBio and Hi-C | Bitter gourd [41] (M. charantia) | OHB3-1 | 11 | 329.99 | 9898.00 | 25.37 | 291.70 (96.27%) | 96.40 | 26277 | 96.40 | 52.52 | 26277 |
| 2020 | Illumina and PacBio | Bitter gourd [42] (M. charantia) | 'Dali-11' | 11 | 293.60 | 62.60 | 3.30 | 251.30 (85.50%) | 96.70 | 26277 | 96.70 | 41.50 | 26277 |
| 2020 | Illumina and PacBio | Silver-seed gourd [36] (Cucurbita argyrosperma ssp. sonorica) | | 20 | 255.20 | 1205.50 | 12.10 | 98.80 | 33829 | 92.80 | 30592 | 92.80 | 30592 |
| 2020 | Illumina and PacBio | Silver-seed gourd [36] (Cucurbita argyrosperma ssp. argyrosperma) | SMH-JMG-627 | 20 | 231.60 | 447.00 | 11.70 | 99.97 | 27998 | 93.20 | 27998 |
| 2021 | Illumina, SMRT, Hi-C, and BioNano optical mapping | Cucumis hystrix [26] | | 12 | 297.50 | 220.95 | 14.06 | 268.90 (90.4%) | 93.50 | 23864 | 93.50 | 23864 |
| 2021 | Illumina, SMRT, Hi-C, and BioNano optical mapping | Cucumis × hystiopsis [27] | | 19 | 540.75 | 6596.00 | 27.20 | 525.78 (97.23%) | 490.71 (93.33%) | 46857 | 50.98 | 46857 |
| 2021 | SMRT and Hi-C | Cucumis metuliferus [28] | | 12 | 329.00 | 2900.00 | 14.06 | 316.82 (97.99%) | 316.82 (97.99%) | 29214 | 42.63 | 29214 |
| 2021 | SMRT and Hi-C | Melon [28] (Cucumis melo ssp. agrestis) | IVF77 | 12 | 364.00 | 490.00 | 28.40 | 24317 | 91.00 | 23541 | 95.50 | 44.99 | 23541 |
| 2021 | Illumina, SMRT | Bottle gourd [8] (Lagenaria siceraria) | 'Hangzhou Gourd' | 11 | 297.00 | 11200.00 | 28.40 | 29214 | 95.50 | 23541 | 95.50 | 44.99 | 23541 |
| 2021 | Nanopore and Hi-C | Chayote [46] (Sechium edule) | | 14 | 608.17 | 8400.00 | 46.56 | 606.42 (99.71%) | 598.48 (98.41%) | 28237 | 65.94 | 28237 |

BUSCOs, Benchmarking Universal Single-Copy Orthologs; SMRT, single-molecule real-time; Hi-C, high-throughput chromosome conformation capture.
differentiation after the first shared WGD event. Among these 17 species, the first divergent species appears to be luo-han-guo followed by bitter gourd [2, 34–37]. The Sicyoeae branch containing sponge gourd, ridge gourd, snake gourd, and chayote diverged sequentially [45, 46]. Species belonging to Benincaseae and Cucurbiteae form the sister clades. The Benincaseae tribe is represented by the four successively divergent genera of Cucumis, Benincasa, Lagenaria, and Citrullus [34, 37], and the Cucurbiteae tribe is represented by four Cucurbita species with the sister pairs of Cucurbita moschata and Cucurbita argyrosperma grouped with Cucurbita pepo and Cucurbita maxima in succession [34, 35] (Fig. 1). Although the divergence times among these cucurbit crops have been estimated using a Bayesian method [2], the exact divergence time of each Cucurbitaceae species remains unclear.

The history of the speciation events has been reported in several studies on genomic research and sometimes there is a conflict of the estimated species divergence time [30, 34–37, 45, 46], which may be affected by the species representativeness, method, fossils, and confidence interval used in estimating the time. For example, the divergence between cucumber and melon has been variously estimated at 8.4–11.8 (the median value is 10.1) Mya [23, 30, 37, 48]. However, according to the research of Ma et al. [45], Fu et al. [46], and Sun et al. [34], the two species (cucumber and melon) diverged ~5–12, 4–14, and 6.06–6.94 Mya, respectively. Therefore, estimates of the divergence between cucumber and melon range from about 4 to 14 Mya. This information is summarized in Table 2.

**Genes associated with important agronomic traits**

With the development of the whole-genome sequences of Cucurbitaceae, a large number of coding genes have been annotated and genes related to fruit and vegetable quality traits have begun to be identified. A wide range of important phenotypic and agronomic traits of Cucurbitaceae plants include pathogen resistance, fruit size, mass, color, texture, length, shape, rind form, ripening behavior, sugar content, bitterness, flavor and aroma, sex determination, and tendrils [12, 24, 32]. Population analysis and genome-wide association studies (GWAS) on diverse species accessions has contributed to the identification of a number of candidate genes controlling desirable fruit and vegetable traits [24]. This provides information for effective breeding strategies and is conducive to the development of high-quality, resilient elite cultivars of Cucurbitaceae species [23, 25].

**Resistance genes**

Plant resistance (R) genes are among the most important targets for plant breeding programs and have been the object of intense research. R genes can activate plant defense systems to restrict pathogen invasion and improve plant resistance against major diseases [49]. The major resistance genes have been identified in various Cucurbitaceae species. Among these genes, those encoding the nucleotide-binding site leucine-rich repeat (NBS-LRR) proteins are related to effector-triggered immunity, which is a significant component of
Table 2. Reported estimates of divergence and evolution of members of the Cucurbitaceae.

| Cucurbitaceae species | Divergence time (Mya) | Reference | Comprehensive viewpoint (Mya) |
|-----------------------|-----------------------|-----------|-------------------------------|
| Cucumis sativus and Cucumis melo | 5–12 | 45 | 4–14 |
|                        | 8.4–11.8               | 30        |                              |
|                        | 4–14                   | 46        |                              |
|                        | 10.1                   | 37        |                              |
|                        | 6.06–6.94              | 34        |                              |
|                        | 12.59                  | 28        |                              |
|                        | 9                      | 44        |                              |
|                        | 8.2–10.0               | 42        |                              |
|                        | 9.63                   | 40        |                              |
|                        | 6.8                    | 39        |                              |
|                        | 9.6                    | 26        |                              |
|                        | 10                     | 30        |                              |
| Cucumis hystrix and Cucumis sativus | 4.5 | 26 | 4.5 |
| Cucumis metuliferus and Cucumis melo | 17.85 | 28 | 17.85 |
| Citrullus lanatus and Lagenaria siceraria | 14–27 | 45 | 10–30 |
|                        | 10.4–14.6              | 30        |                              |
|                        | 12–30                  | 46        |                              |
|                        | 13.8                   | 37        |                              |
|                        | 18.34–19.75            | 34        |                              |
|                        | 16                     | 28        |                              |
|                        | 13.0–15.7              | 42        |                              |
|                        | 15.11                  | 40        |                              |
|                        | 14.9                   | 39        |                              |
|                        | 21.4                   | 26        |                              |
|                        | 10–14                  | 30        |                              |
| B. hispida and Citrullus lanatus/Lagenaria siceraria | 16.3 | 37 | 16.3–18.1 |
|                        | 18.1                   | 40        |                              |
|                        | 16.8                   | 39        |                              |
| Siraitia grosvenorii and Citrullus lanatus | 40.9 | 44 | 40.9 |
| Momordica charantia and other | 48–77 | 45 | 29.2–96 |
|                        | 29.2–41                | 30        |                              |
|                        | 39–96                  | 46        |                              |
|                        | 36.1                   | 37        |                              |
|                        | 44.1 ± 14              | 35        |                              |
|                        | 34.94–37.24            | 34        |                              |
|                        | 33.3–40.4              | 42        |                              |
|                        | 44.06                  | 40        |                              |
|                        | 41.6                   | 39        |                              |
|                        | 49.8                   | 26        |                              |
| Cucurbita maxima and Cucurbita moschata | 3.04–3.84 | 34 | 3.04–7.3 |
|                        | 5.3–7.3                | 42        |                              |
|                        | 4.81                   | 40        |                              |
| Cucurbita maxima and Cucurbita pepo | 13.9 | 28 | 13.9 |
| Cucurbita moschata and Cucurbita pepo | 3.9–5.4 | 42 | 3–16 |
|                        | 3–16                   | 46        |                              |
|                        | 3–13                   | 45        |                              |
|                        | 6.3                    | 39        |                              |
| Cucurbita moschata and Cucurbita angyrosperma | 3.98 ± 1.7 | 35 | 3.98 ± 1.7 |
| T. anguina and Sechium edule | 27–45 | 46 | 27–45 |
| Luffa acutangula and Luffa cylindrica | 7.97 | 40 | 7.97 |
| Luffa cylindrica and T. anguina | 33–47 | 45 | 29–55 |
|                        | 29–55                  | 46        |                              |

Plant disease resistance [50]. A total of 44 NBS-LRR (NLR) genes, consisting of 26 coiled-coil (CC)-NBS-LRR (CNL) and 18 Toll interleukin receptor (TIR)-NBS-LRR (TNL) genes, have been identified in watermelon [31]. The number of NLR genes identified in cucumber, melon, wax gourd, Cucurbita maxima, Cucurbita moschata, and bitter gourd are 74, 84, 82, 30, 57, and 78, respectively [34, 37].

Research on the aphid resistance of cucumber cultivar ‘EP6392’ showed that 8 of the 49 DEGs may be relevant to aphid resistance [51]. The volatile (E,2)-2, 6-nonadienal (NDE) is involved in resistance to a number of bacteria and fungi in cucumber [52]; several EIF4E and EIF4G genes were found to be resistant to plant RNA virus infections, and two At (glyoxylate aminotransferase) gene homologs conferring potential resistance to downy mildew have also been identified [12]. Interestingly, an EIF4E gene found in melon mediates recessive resistance against melon necrotic spot virus [53–55], and
the increased expression of two glyoxylate aminotransferase (At1 and At2) genes was found in wild melon genotypes, which may contribute to their resistance to downy mildew [56].

The most prevalent viruses that have a significant impact on the production of cucurbit crops are aphid-transmitted viruses in the Potyviridae family, including papaya ring-spot virus watermelon strain (PRSV-W), zucchini yellow mosaic virus (ZYMV), and watermelon mosaic virus (WMV) [57–64]. Of these, PRSV-W is one of the most destructive viruses that infect cucurbits worldwide [65–67]. The bottle gourd USVL5VR-Ls line is resistant to PRSV-W [68], and resistance is determined by Prs, an unidentified dominant monogenic locus [30]. An NBS-LRR gene (RGH10) was shown to confer PRSV resistance in melon [69]. Research has showed that ethylene signaling may participate in the PRSV resistance mechanism in cucurbits. AP2/ERF transcription factors (TFs) have been reported as the basis of plant defense mechanisms against a wide range of pathogens, including viruses, which makes the AP2/ERF gene family a feasible source of candidate genes for Prs [70]. In the snake gourd genome, five R genes potentially involved in the plant–pathogen interaction pathway have been identified [45]. Changes in their expression are associated with the changes in resistance during fruit ripening, which may possibly be related to the resistance of snake gourd to pathogens and insects [45].

Sex determination

In Cucurbitaceae, sex determination is closely related to fruit earliness, yield, and quality [71]. Ethylene stimulates femaleness and is regarded as the main regulatory factor of sex determination [72–74]. Naturally occurring mutations in the genes encoding the corresponding enzymes in the ethylene biosynthesis pathway have a notable impact on sex determination in the Cucurbitaceae [75, 76]. For example, a loss-of-function mutation in a 1-aminocyclopropane-1-carboxylic acid synthase (ACS) gene in melon and cucumber leads to the enhancement of ‘femaleness’ [75, 77]. There seem to be similar mechanisms at play in Cucurbita pepo [78]. In addition, the ACC oxidase gene CsACO2 is essential in female flower formation in cucumber and mutations in this gene confer androecy [79]. Studies have also shown that ethylene receptors are implicated in the regulation of zucchini sex determination [80, 81]. Cucumber and melon are often used to study sex expression in Cucurbitaceae plants [12, 23, 82]. Three major sex determination genes, M, F, and A, have been established in cucumber, and shown to be members of the aminocyclopropane-1-carboxylic acid synthase (ACS) gene family (CsACS1G for F, CsACS2 for M, and CsACS11 for A) [77, 79, 83–86]. Cucumber has a distinctive genetic system for gynoecious sex expression and contains three genes: CsACS1, CsACS1G, and CsMYB [87–90]. Study has revealed that the CsACS1G gene is responsible for production and development of female flowers in cucumber gynoecy conferred by the F locus [91]. However, this gynoecy expression system appears to be unstable, which may be due to unequal crossing over at the copy number variation (CNV)-based femaleness (F) locus [87]. The melon sex determination-related gene Cm-ACS7 and ACS11, and cucumber ortholog Cs-ACS2, as well as Cucurbita pepo ortholog CpACS27A, are crucial regulatory enzymes in the ethylene biosynthetic pathway [77, 92–95]. These genes are vital to the suppression of male organs and development of the female flower [77, 92–95]. In addition, the gynoecious locus CmWIP1 involved in occurrence of gynoecy in melon has also been found to be implicated in sex determination of cucurbits [96–99]. It has two orthologous genes (CpWIP1A and CpWIP1B) identified in Cucurbita pepo [92]. In addition, auxin can regulate sex expression through stimulating ethylene generation [72–74]. Research has suggested that six auxin-related genes and three short-chain reductase or dehydrogenase genes involved in sex determination have higher expression levels in unisexual flowers of cucumber [12]. The identification and functional analysis of these genes have provided valuable information for the study of sex expression in other Cucurbitaceae plants.

Fruit color

The diverse color of fruit is determined by the concentrations and compositions of various pigments, mainly chlorophylls and carotenoids, as well as flavonoids (especially chalcones and anthocyanins). Melon rinds have a variety of colors, including green, white, orange, yellow, variegated, and striped [100]. It is known that β-carotene accumulation can contribute to the orange color, and the accumulation of lutein and other carotenoids contributes mainly to the yellow color of fruit [101], while the carotenoid content of white-fleshed melon and watermelon can be low or negligible [102, 103]. A yellow flavonoid pigment, naringenin chalcone, was identified as the major pigment in mature rinds of ‘canary yellow’ type melons [100]. Similarly, the main carotenoids that accumulate in yellow-fleshed watermelon and zucchini are lutein and β-carotene [104].

The key genes known to be implicated in the carotenoid metabolic pathway play important roles in regulating carotenoid accumulation, leading to changes in pigmentation [105]. The CmPPR1 (EVM0014144) gene may affect carotenoid accumulation and flesh color in melon [106–108]. The CmOr gene controls β-carotene accumulation, resulting in the orange flesh colors in melon fruit [109], while the identified MELO3C003097 gene may serve as a strong candidate for the Wf locus controlling white and green melon flesh [25]. Moreover, two peel-color-related candidate genes, MELO3C003375 and EVM0012228 (CmKFB), have been identified [25]. CmKFB genes negatively regulated the accumulation of naringenin chalcone determining the yellow color of melon rind [110]. The flesh color of Cucurbita moschata and Cucurbita maxima usually appears to be yellow and orange, while zucchini is mainly white and pale
yellow [111–114], \(\beta\)‐Carotene hydrolase (CHYB) and phytoene synthase (PSY) are two main genes affecting the formation of yellow‐fleshed fruit of Cucurbita moschata, Cucurbita maxima, and Cucurbita pepo [113–115], while the carotenoid cleavage dioxygenases 4 (CCD4) gene exerts an important function in the regulation of white pulp in Cucurbita pepo [112]. Ripe M. charantia fruits had higher carotenoid (mainly \(\beta\)-carotene) concentrations [116]. During fruit ripening, increased expression of phytoene synthase (McPSY) and phytoene desaturase (McPDS), associated with carotenoid synthesis, was observed, resulting in carotenoid accumulation in the pericarp and a change of peel color from green to orange [116, 117]. A study in Cucurbita pepo showed that the up-regulated expression of several structural genes involved in carotenoid metabolic pathways probably leads to the increased carotenoid accumulation in ripe fruit [92]. It is well known in tomato that PSY1 is a critically important enzyme that is induced during ripening [118, 119]. In ripening fruit of sweet watermelon, the PSY1 gene may be involved in the transition from pale-colored to red, orange, or yellow flesh through increasing total carotenoid accumulation [32]. Mutation in LCYB may lead to increased lycopene content, since artificial selection of the mutation was shown to be responsible for the red flesh color in most sweet watermelon cultivars [32]. Moreover, CltSST2, a sugar transporter gene, was credited with facilitating carotenoid accumulation in watermelon fruit flesh [32]. During flesh color formation, the up-regulated expression of gene CIPHT4;2 was closely related to increased carotenoid contents in watermelon flesh [107, 120]. In chayote fruit, a number of candidate genes regulating pigment accumulation have also been identified, such as HCAR (7-hydroxymethyl chlorophyll a reductase), regulating chlorophyll content, and \(\beta\)-carotene hydroxylase 2 (CHY2), CCD1, CCD4, and ZEP [46]. These genes may be involved in fruit color production [46]. The up-regulated expression of carotenoid accumulation-related genes may contribute to the increase of carotenoid content, making the fruit turn orange-red after ripening in snake gourd fruit [45].

Fruit size, shape, and texture

There are many factors that affect the formation of fruit shape, and their interaction and coordination eventually lead to differences in fruit shape. Various studies have reported a variety of classical and newly identified key genes related to fruit shape, mainly including SUN, OFP, WOX, YABBY, AP2, and auxin transporters [8, 121–124]. Apart from these well-known genes, sugar signaling and metabolism have been suggested to be related to cell division and growth, which can influence organ shape [125]. Through GWAS analysis, a strong association signal related to fruit shape in watermelon was identified near the ClFS1 (Cla97C03066390) gene controlling fruit elongation [126]. In addition, other genes or proteins related to fruit shape are also found in different plants, such as the TONNEAU1 recruiting motif protein (TRM5), the AP2/ERF transcription factor (AP2a) gene in tomato [127, 128], and the CAD1 gene belonging to the LRR-RLK family in peach [129].

The fruit shapes of Cucurbitaceae plants are diverse, and some genes controlling their shape variation have been identified. Quantitative trait locus (QTL) analysis for cucumber showed that the round fruit shape in Wt7239 is controlled by two QTLs, FS2.1 and FS1.2, containing the tomato homologous genes SITRM5 (GSTM5) and SUN (CsSUN25–26,27a), respectively [128, 130]. The deletion of the rst exon of FS1.2 in cucumbers results in the formation of round fruits [130]. In another study, FS5.2 greatly influenced the formation of round fruit in Wt1767 cucumber [130]. Watermelon fruits have three major shapes: elongate (OO), oval (Oo), and spherical (oo), controlled by a single, incompletely dominant gene [126]. A candidate gene, Cla011257, on chromosome 3 related to watermelon fruit shape (ClFS1) was identified and results suggested that Cla011257 might control spherical fruit shape and a deletion of 159 bp in Cla011257 may lead to elongated fruit in watermelon [126]. The wax gourd fruit shapes are mainly long cylindrical, cylindrical, and round [131]. During ovary formation, the expression levels of Bch02G016830 (designated BFS) in round wax gourd fruit are significantly higher than in long cylindrical fruits [131]. Therefore, BFS might be a candidate gene for fruit shape in wax gourds [131]. Variations in BFS might slow down cell division at the ovary formation stage and may contribute to the regulation of wax gourd fruit size [131]. In Cucurbita pepo, a single gene, Di, controls the disk fruit shape, which is dominant over spherical or pear-shaped fruit [132]. In Cucurbita moschata, the gene Bn controls butternut fruit shape and is dominant to bn for crookneck fruit shape [133]. In addition, sex expression has pleiotropic effects on cucumber and melon fruit shape [140, 134]. A 14-bp deletion in CsACS2, the candidate gene for the monoecious (m) locus in cucumber, resulted in elongated fruit shape in cucumber [95]. The pleiotropic effect of sex expression on fruit shape is also well established in melon [134].

Plant hormones have been showed to contribute to the regulation of fruit size and development [135]. Ethylene participates in many plant development processes and it serves as a triggering signal to initiate climacteric fruit ripening [136, 137]. The CpACS27A gene in Cucurbita pepo is the homologous gene of CmACS7 (MELO3C015444) in melon, which is involved in ethylene synthesis and sex determination and also influences fruit length [75, 108]. Auxin plays a critical role in cell expansion during fruit development stages [138–140] and the role of the main regulators of auxin—auxin response factors (ARFs)—in cell division and growth have been well established [140, 141]. A total of 56 ARF genes were identified in bitter gourd [142], but in other families the number can vary considerably. It has been suggested that auxin-responsive GH3 family genes, auxin-responsive protein (I AA), and SAUR family proteins may be associated with chayote fruit enlargement [46], and the up-regulated...
expression of auxin-related genes may be involved in snake gourd fruit elongation [45]. SAUR was reported to be implicated in the regulation of plant growth and development through promoting cell expansion [143–145], Bhi10G001538 and Bhi10G000196 may be important candidate genes contributing to large fruit during wax gourd domestication [37], and Bhi10G000196 is orthologous to the tomato gene SIFIN (Solyc11g064850) responsible for enlarged tomato fruit [146]. In addition, four WUSCHEL TFs have been identified in Cucurbita pepo [92], which affect fruit size [147, 148].

During fruit growth, development and ripening, there are many changes to cell wall structure and properties in cell wall biogenesis and modification, cell expansion, unidirectional elongation, and fruit softening [149, 150]. Numerous different types of cell-wall-modifying enzymes have been identified as being involved in the development and ripening processes of many fruits, including the pectin-modifying enzymes [polygalacturonase (PG), pectinesterase (PE), pectate lyase (PL), and β-galactosidase (β-GAL)] and the hemicellulose/cellulose-modifying enzymes [β-1,4-glucanase, xyloglucan transglycosylase/hydrolase (XTH) and expansin (EXP)], which together lead to changes in fruit texture by regulating the structure of cell wall polymers and influence fruit ripening [137, 151]. The increased expression of β-1,4-glucanase or enhanced enzyme activity is usually associated with fruit softening [75]. In addition, six genes (three pectinesterase genes, two gibberellin 20 oxidase 1-B-like genes, and one pectate lyase-like gene) involved in cell wall biosynthesis have been identified that may play important roles in determining epidermis thickness in the melon [24]. Regulation of the expression of many DEGs related to cell wall modification may be associated with fruit texture changes in snake gourd, including β-galactosidase 10/5-like, cellulose synthase-like protein, endoglucanase 10/11/17-like, expansin-A4/A10-like, β-glucosidase 18-like, and pectinesterase 53 [45]. Moreover, polygalacturonase, pectinesterase, and cellulose synthase-like protein B4 may affect cell wall properties and fruit texture during chayote development [46]. Expansins are cell wall proteins regulating cell size and fruit growth in plants, and are also highly expressed during fruit development and ripening [152, 153]. Although they have no catalytic activity, the expansins appear to induce loosening of bonds between cellulose and hemicellulose in the cell wall, leading to ‘polymer creep’ within the cell wall during growth, resulting in cell enlargement or shape change [137]. Also, expansins enable cell expansion and fruit softening by triggering the loosening of the cell wall [154]. Expansin-A12 is thought to be implicated in melon fruit size [24], and expansin-like B1, identified in the chayote fruit, may induce plant cell wall extension, with increased transcripts contributing to rapid fruit enlargement [46].

Other genes involved in cell division and cell cycle regulation can also directly influence the growth rate of plant tissues and determine the final size of plant organs [155]. A total of six DEGs related to the regulation of cell division and the cell cycle were identified in bottle gourd [156]. Furthermore, the study of melon showed that L-ascorbate oxidase (AAO) could play a role in the late stage of fruit development, associated with the change in fruit size [157]. Differential expression of the gene was also found in Cucurbita pepo [92], snake gourd [45], and chayote [46]. In Cucurbita pepo, up-regulated expression of the CpoVATE gene acting as a repressor of growth was observed in the small-fruit ‘Munchkin’, which showed that OVATE plays a key role in shorter fruit [158]. Similarly, the hexokinase (CphHXK-1) and CpfW2.2 genes were also found to contribute to a reduction in fruit size [158].

**Fruit taste**

There are three major components, including acidity, sugar, and volatile flavor compounds, that together contribute to the overall taste of fleshy fruit [159]. The PH gene (CmPH) identified in melon has an important regulatory effect on fruit acidity [159], and numerous genes involved in the citrate acid cycle that may influence the accumulation of organic acids have also been identified in melon [160]. The ClBt gene in watermelon and CsBt in cucumber regulate fruit bitterness [5, 32, 161] and volatile (E,Z)-2,6-nonadienal (NDE) confers on cucumber its ‘fresh green’ flavor [162], while CmTHAT1 (thiol acyltransferase, EVM0016460) affects fruit flavor [24, 108].

Sugar accumulation is the main factor that contributes to the sweet taste, which is particularly important in the fruit ripening process of melon and watermelon. Two candidate genes, EVM0015625 and EVM0019658, have been suggested to be responsible for sugar accumulation in melon and the β-glicosidase and α-1-fucosidase genes are related to the synthesis and transportation of sugars [24]. In melon fruit, a total of 63 genes may be involved in the sugar metabolism pathway [23], and enzymes considered to be involved in regulating sugar biosynthesis, unloading, transport, and metabolism processes during watermelon flesh development include neutral invertase, α-galactosidase, sucrose phosphate synthase, insoluble acid invertase, soluble acid invertase, UDP-glucose 4-epimerase, and UDP-galactose/glucose pyrophosphorylase [31]. An alkaline α-galactosidase gene (CiAGA2) was suggested to be related to the accumulation of sugar in watermelon pulp by promoting the metabolism of raffinose into glucose, fructose, and sucrose [32, 163–165]. The roles of vacuolar sugar transporter ClVST1, hexose transporter ClSWEET3, and tonoplast sugar transporter CTS12 in the sugar accumulation of watermelon fruit are well established [165]. ClVST1 is responsible for glucose and sucrose efflux and unloading in the watermelon fruit [166]. The key transporter protein CTS12 contributes to the accumulation of sucrose, fructose, and glucose in the vacuole of watermelon fruit cells [167]. Their expression levels are positively correlated with watermelon fruit sugar content and their overexpression increased fruit sugar accumulation of watermelon flesh [168]. In addition,
the overexpression of an ortholog of CiTST2 (CmTST2) in melon fruit could increase sugar content [168]. TF genes putatively implicated in sugar accumulation include a bZIP gene, namely Cla014572, which functions as a key regulatory factor of sugar accumulation during fruit development [31, 169]. Further work on the identification, differential expression, and functional analysis of these genes will contribute to the understanding of fruit flavor of Cucurbitaceae plants. The catabolism of several amino acids plays a central role in the production of aroma compounds in melon [170]. Valine, leucine, and isoleucine are implicated in the biosynthesis of branched-chain esters [171], and tyrosine and phenylalanine participate in the biosynthesis of aromatic esters [172]. Ethylene can enhance the levels of these amino acids to promote synthesis of esters, thus affecting melon flavor [170], and ethylene may also enhance aminotransaminase (AT) activity by increasing the expression of CmBCAT1 and CmArAT1, whose gene products convert branched chain amino acids into aroma volatiles through amino acid aminotransferases [172, 173]. The key role of the two genes in the biosynthesis of melon aroma volatiles is well documented [172]. Sulfur-containing aroma volatiles make an important contribution to the distinctive aroma of melon and other fruits [173] and thioether esters greatly promote the fruity aroma of melon fruit [174, 175]. L-Methionine was postulated to be a precursor of aroma volatiles in melon fruit [175]. Two distinct parallel pathways for L-methionine catabolism, a transamination route involving the action of an L-methionine aminotransferase and a γ-lyase route involving the action of an L-methionine-γ-lyase activity encoded by melon gene CmMGL is involved in the formation of melon aroma volatiles [173]. In addition, sulfur-containing esters may also be synthesized from cysteine [170].

The cucurbitacins are plant triterpenoids that form the bitter compounds predominant in the Cucurbitaceae family and impart a bitter taste in cucumber, zucchini, melon, pumpkin, and other plant foods [5, 161, 176]. To date, many cucurbitacins, including cucurbitacins A–L, O–T, and several others, have been discovered in plants (https://en.wikipedia.org/wiki/Cucurbitacin). Several studies have shown that they exhibit wide-ranging pharmacological activities, such as cytotoxic, hepatoprotective, purgative, anti-inflammatory, anti-infectious, antidiabetic, antitumour and anticancer effects [177–180]. In addition, cucurbitacin I can suppress cell motility through interfering indirectly with actin dynamics [181]; cucurbitacin B and cucurbitacin I could be beneficial in suppressing adipocyte differentiation and preventing metabolic diseases [182]; and the efficacy of cucurbitacin R and dihydrocucurbitacin B on the immune system has also been recognized [183].

The precursors of cucurbitacin triterpenoids are synthesized through the mevalonate pathway [184] and cucurbitadienol is produced by cucurbitadienol synthase, forming the basic skeleton of cucurbitane triterpenoids [185] (Fig. 2). Cucurbitacins C (CuC), B (CuB), and E (CuE) are the main bitter substances isolated from cucumber [5], melon [186], and watermelon [187], respectively. The biosynthesis pathway of CuC has been described by Shang et al. [5]; nine CuC biosynthetic enzymes (CsBi, seven CYPs, and CsACT) were identified and four catalytic steps were elucidated. Eight CuB (CmBi, six CYPs, and CmACT) and 10 CuE biosynthetic enzymes (CtBi, 8 CYPs, and CIACT) have also been identified in melon and watermelon, respectively [161]. The cucurbitacin biosynthetic enzymes (Bi, eight CYPs, and ACT) have also been identified in Luffa acutangula and Luffa cylindrica [39]. The biosynthesis pathway of cucurbitane triterpenoid in bitter gourd was reported by Cui et al. [42]. The identification of these bitter genes has contributed to understanding the regulatory and biochemical variations of cucurbitacins and provided important information for molecular breeding for taste improvement.

Transcription factors involved in fruit growth and ripening

Many TF families have important effects on fruit development [188–190]. Myeloblastosis (MYB) proteins are one of the largest TF families in plants and are widely involved in diverse plant-specific processes, such as plant organ development, signal transduction, secondary metabolism, and multiple stress responses [191–194]. In cucumber, two MYB genes, CsMYB6 (Csa3G824850) and CsSTRY (Csa5G139610), have been reported to negatively regulate fruit spine or trichome initiation [195]. Other research has shown that the CsSTRY not only regulates fruit spine or trichome formation, but also plays a negative regulatory role in anthocyanin synthesis [196]. Moreover, CsMYB60 is a key regulatory gene that determines fruit spine color in cucumber, and is a good candidate for the B (black spine) gene controlling the black fruit-spine trait, which regulates the pigmentation of black spines [197, 198]. A total of 162 MYB genes have been identified in watermelon [199].

The GRAS family constitutes one of the major plant-specific TF families that are related to plant growth, development, cell signaling, and stress tolerance [200]. It has been reported that a total of 237 GRAS genes were identified in six Cucurbitaceae crop genomes. The number of GRAS genes was little different among these species, including Cucumis sativus (37), Citrullus lanatus (37), and Lagenaria siceraria (37) [201, 202], while the number present in Cucurbita moschata (55) was considerably greater. It is known that silencing the S1GRAS2 gene can reduce fruit weight during tomato fruit development [203]. The study proposed that several genes homologous to S1GRAS2 (CmoCh09G009100.1, CmoCh01G012140.1, MELO3C018144T1) among these GRAS genes might potentially function in fruit development [203].

The NAC domain genes are also one of the largest TF families in plants [204]. A total of 81 genes encoding 92
proteins of the NAC-domain family have been identified in the melon genome [204, 205]. They play an important part in the regulation of fruit ripening in different plants and CmNAC-NOR, a melon NAC gene family member, is a homolog of tomato Nor gene (SinAC-NOR), involved in the climacteric fruit ripening process [136, 204, 206]. The NAC gene SlNAC4 can influence carotenoid accumulation and ethylene synthesis and is a positive regulator of fruit ripening in tomato [206]. The precise roles of the crucial tomato ripening ‘master regulators’, including MADS-RIN, NAC-NOR, and SPL-CNR, have been re-evaluated and it turns out that their severe ripening-inhibition phenotypes result from gain-of-function mutations [136]. Nevertheless, in the wild type, these regulators, plus Nor-like1 and other MADS and NAC genes, together with ethylene, play major roles in changes in color, flavor, texture, and ripening progression through promoting the full expression of related genes [206, 207]. MADS-box genes have been reported to regulate fruit expansion and ripening processes in melon [205, 208]. In addition, there are many other TFs involved in the regulation of fruit ripening, including the positive regulators TAGL1 [209] and LeHB-1 [210] and the negative regulators LeERF6 [211] and LeAP2a [212].

Transcriptomics

Transcriptome analysis has become an effective approach to understanding the gene networks that govern quality and developmental processes (Fig. 3) and can aid in identifying and exploiting superior cultivars with desirable traits, thus accelerating the Cucurbitaceae plant-breeding process. The transcriptome sequences of many Cucurbitaceae plants, including Cucurbita maxima [35], Cucurbita moschata [35], Cucurbita argyrosperma [35], bottle gourd [30], wax gourd [37], chayote [46], snake gourd [45], watermelon [31, 32], and zucchini [29], are available in the Sequence Read Archive (SRA) database of NCBI. These data provide important information on protein-coding gene prediction, new gene discovery, and gene functional annotation. In addition, transcriptome sequencing has been employed to investigate the
molecular basis of the development of many fleshy fruits in Cucurbitaceae species, including cucumber [152, 213-215], melon [216–218], watermelon [219], bitter gourd [150], Momordica cochinchinensis [220], bottle gourd [156], zucchini [92, 158, 221], pumpkin [222, 223], wax gourd [224], snake gourd [45], and chayote [46]. Many DEGs related to fruit quality have been identified and Table 3 shows the integrated gene information derived from the transcriptome data of Cucurbitaceae plants.

**importance of genome resequencing for the development of molecular breeding**

Whole-genome resequencing technology has been used to investigate wide germplasm resources. Resequencing of multiple materials from different crop species has helped reveal the domestication history of cucurbit crops and candidate genes or loci influencing agronomic traits. Important cucurbit crops that have been resequenced include Citrullus lanatus [31, 32], Cucumis sativus [15], Cucumis melo [24, 25, 225], B. hispida [37], M. charantia [41], and Lagenaria siceraria [8]. Resequencing and provision of large-scale germplasm resources can be applied to population genomic analyses and GWAS to identify QTLs. Genome-wide single-nucleotide polymorphism (SNP) markers have been widely used in molecular breeding for mapping of important fruit quality trait genes and can contribute to the discovery of candidate loci or key genes and molecular markers associated with important traits in cucurbits for crop improvement (Table 4).

A genome variation map for cucumber fruit was obtained through deep resequencing of 115 cucumber lines and a region containing a gene related to the loss of bitterness in cucumber fruit was identified [15]. The QTL mapping of cucumber also identified eight QTLs related to leaf size or fruit length [15]. Moreover, a natural genetic variant in a $\beta$-carotene hydroxylase 33 gene (CsaBCH1) that resulted in accumulation of $\beta$-carotene and formation of orange fruit endocarp was identified, which could be helpful in obtaining varieties with higher nutritional value [15]. In Payzawat melon, six structural gene variants potentially controlling the thickness of the epidermis were identified by analyzing the QTLs related to epidermis thickness [24]. In addition, Zhao et al. [25] reported a comprehensive map of the melon genomic variation that originated from the resequencing of 1175 accessions, and GWAS studies for 16 agronomic traits identified 208 loci markedly related to fruit quality, mass, and morphological characters. This study proposed that the strong differentiation between Cucumis melo and Cucumis agrestis may contribute to breeding. Watermelon breeding has mainly focused on fruit quality traits, particularly, sweetness, flesh color, and rind pattern, which has led to the narrow genetic base of watermelon [32]. In 2013, Guo et al. [31]
| Cucurbitaceae | Color-related genes | Texture-related genes | Aroma-, flavor-, and taste-related genes | Plant hormone-related genes | Key transcription factors |
|--------------|---------------------|----------------------|----------------------------------------|-----------------------------|---------------------------|
| Cucumber     | δ-carotene hydroxylase (BCH), β-carotene 3-hydroxylase (BCH), β-carotene isomerase (BISO), carotenoid cleavage dioxygenase 7 (CCD7), 9-cis-epoxy-carotene dioxygenase (NCED) | β-galactosidase (β-Gal), β-glucosidase (β-Glu), β-amylase 1/3 (BMV1/3), cellulase 3 (CL3), pectin lyase (PL), pectinesterase (PE), pectin methylesterase 3 (PME3), pectinacetylemethylesterase (PAME), xylanoglucan-xylanotransferase (XET5), expansin (EXP), cellulose synthase (CesA) | terpene synthase 21 (TPS21), lupeol synthase (LUS), glutamate dehydrogenase 2 (GDH2), lipoxygenase (LOX), phenylalanine ammonia-lyase 2 (PAL2), alcohol dehydrogenase 1 (ADH1), sucrose synthase 4/5 (SUS4/5), β-aminin synthase (β-AS) | 1-aminocyclopropane-1-carboxylate synthase 3/10 (ACS3/10), gibberellin-responsive protein, histidine phosphotransfer protein (HP), AUX1, Aux/IAA, small auxin-up-regulated RNA (SAUR), ent-kaurenoic acid (KAO), gibberellin 20-oxidase (GA20ox), gibberellin 2-oxidase (GA2ox), gibberellin insensitive dwarf 1 (GID1), auxin-responsive GHI family protein (GHI), gibberellin-regulated family protein (GASA), auxin-responsive protein, auxin-induced protein 13, ethylene insensitive 3 (EIN3), ethylene response factor (ERF), gibberellin 2-oxidase 8 (GA2ox) | AP2/ERF, GRAS, HSF, LPY, MADS, NAC, WRKY, YABBY, Zinc finger protein, k2IP, MYB, TCP, WD40, HHL, SBP, NF-YA, AUX/IAA |
| Melon        | phytene synthase (PSY), carotenoid hydroxylases (CYP97A3), 9-cis-epoxy-carotene dioxygenases (NCED), abscisic acid 8'-hydroxylase (CYP707A) | carotenoid isomerase (CRTISO), carotenoid hydroxylases (CYP97A3), 9-cis-epoxy-carotene dioxygenases (CCD), abscisic acid 8'-hydroxylase (CYP707A) | sucrose phosphate synthase 2 (CmSPS2), sucrose synthases (CmSUS1, CmSUS2 and CmSUS-LIKE1), hexokinases (CmHK2 and CmHK3), fructokinase 3 (CmFK3), acid invertases 2 (CmAIN2), cell wall invertases (CmCIN2 and CmCIN3), phosphoglucosamine isomerase (CmPGIcyt), α-carotidase (GAL2), phosphoamynolpyruvate carboxylase (CmPK1, CmPK2 and CmPK3), cytosolic NADPH-dependent isocitrate dehydrogenases (IDH1 and IDH2), α-gluoside dehydrogenase 1 (MD1, MD2), acetaldehyde 1 (ACO1), 2-oxoglutarate dehydrogenase (OGDH), pyruvate dehydrogenase (PDH) | No data | AP2/EREBP, Constans-like zinc finger, C2H2 zinc finger, GOLDEN2-like, MYB, HHL, WRKY |
| Watermelon   | phytene synthase 1 (PSY1), lycopene, β-cyclase (LCYB), 9-cis-epoxy-carotene dioxygenase 5 (NCED5), β-carotene hydroxylase (BCH), carotenoid β-ring hydroxylase (CYP97A3), carotenoid cleavage dioxygenase (CCD) | pectin methylesterase (PEM), pectinesterase (PE), proline-rich proteins (PRPs), fasciclin-like arabinogalactan proteins (FLAs), xylanoglucan endotransglycosylases (XETs), early nodulin-like proteins (ENODs), S-adenosyl methyltransferase (SAMDC), β-D-glucosidase (β-Glu), β-galactosidase (β-Gal), cellulose synthase (CesA), endo-1,4-β-glucanase (EG), endoglucanase (EG) | δ-factye 2 stem C-5 desaturase (S-DES), phenylalanine ammonia-lyase (PAL), pyruvate decarboxylase (PDC), malate dehydrogenase (MD), sucrose synthase (SUS), sucrose-phosphate synthase (SPS), ascorbate peroxidase (APX), squalene synthase (SQS) | ethylene response factor 1 (ERF1), gibberellin 20-oxidase (GA20ox), Gibberelin regulated protein (GASA), auxin-repressed protein ARPI (ARPI), abscisic acid response protein, Aux/IAA protein, auxin response factor 2 (ARF2), auxin-repressed protein (ARP) | AP2/ERF, k2IP, MADS, MYB, NAC, WRKY |
| Cucurbitaceae     | Color-related genes                                      | Texture-related genes                                | Aroma-, flavor-, and taste-related genes                                      | Plant hormone-related genes                                      | Key transcription factors |
|-------------------|----------------------------------------------------------|------------------------------------------------------|-----------------------------------------------------------------------------|-------------------------------------------------------------------|--------------------------|
| Bitter gourd      | phytene synthase (FSY), zeta-carotene desaturase (ZDS), 15-cis-phytene desaturase (PDS), lycopene β-cyclase (LCYB), lycopene-ε-pyrone-cyclase (LCYE), polygalacturonase isomerase (CPRISO), carotene ε-pyrone monoxygenase (CYP97B1), zeaxanthin epoxidase (ZEP), violaxanthin de-epoxidase (VDE), zeta-carotene isomerase (ZISO), β-carotene 3-hydroxylase (BCH), xanthoxin dehydrogenase (ABA2), flavonol synthase (FLS), chalcone synthase (CHS) | Pectinesterase (PE), pectate lyase (PL), β-galactosidase (β-Gal), β-amylase (BMY), β-glucosidase (β-Glu), α-mannosidase (MANA), polygalacturonase 2 (PG2) | sucrose synthase (SUS), phosphoenolpyruvate carboxylase (PEPC), (S)-linoleic synthase (TPS14), lipoxygenase (LOX), alcohol dehydrogenase (ADH), glutamate synthetase (GS), glutamate decarboxylase (GAD), pyruvate decarboxylase (PDC), phenylalanine ammonia-lyase (PAL), β-amyrin synthase (β-AS) | 1-aminocyclopropane-1-carboxylate synthase (ACS), gibberellin 2-oxidase (GA2ox), gibberellin 20-oxidase (GA20ox), auxin-responsive protein IAA (IAA), auxin response factor (ARF), gibberellin receptor GID1 (GID1), abscisic acid receptor PYR/PYL (PYR/PYL), Jasmonic acid-amino synthetase (JAR1), ethylene receptor (ETR), serine/threonine-protein kinase CTR1 (CTRI), ethylene-insensitive protein 2/3 (EIN2/3), ethylene-responsive transcription factor 2 (ERF2), small auxin up RNA (SAUR), auxin-binding protein (ABC), auxin induced, auxin efflux carrier component 8, cytokinin dehydrogenase (CXX), gibberellin 3-β-dioxigenase 1 (GA3ox1) | AP2, AP2/ERF, Dof, NAC, WRKY |
| Bottle gourd      | No data                                                  | endoglucanase (EG), expansin (EXP), galactoside 2-α-L-fucosyltransferase 2 (FUT2), galacturonosyltransferase-like 2 (GATL2), xyloglucan endotransglycosylase/hydrolase 2 (XTH2), xyloglucan glycosyltransferase 5 (CSLCS), xyloglucan endotransglycosylase/hydrolase protein (XTH) | sucrose-phosphate synthase 4 (SPS4), sucrose synthase 5 (SUS5) |                                                                 |                                                                 | APRR2, bHLH, bZIP, ERF, MYB, MYC, RAD, TFIIH, WRKY |
| Zucchini          | phytene synthase (PSY), phytene desaturase (PDS), β-carotene hydroxylase (BCH), carotenoid cleavage dioxygenase (CCD), carotenoid isomerase (CPRISO), zeta-carotene desaturase (ZDS), chalcone synthase 2 (CHS2), zeaxanthin epoxidase (ZEP) | Pectinesterase (PE), pectate lyase 12 (PL12), polygalacturonase (PG), glucan endo-1,3-β-D-glucosidase (BGL2), cellulose synthase-like protein D5 (CSDL5) | linolate 9S-lipoxygenase 6 (LOX6), glutamate dehydrogenase 2 (GDH2), linolate 13S-lipoxygenase 2-1 (LOX), alcohol dehydrogenase (ADH), granule-bound starch synthase (GBSS), sucrose synthase 5 (SUS5) | 1-aminocyclopropane-1-carboxylate synthase 3/4 (ACO3/4), ethylene insensitive 2/3 (EIN2/3), ethylene response 1/2 (ETR1/2), ethylene response factor (ERF), 1-aminocyclopropane-1-carboxylate synthase (ACS), gibberellin 2-oxidase (GA2ox), auxin-induced protein, auxin response factor (ARF), auxin-responsive protein IAA (IAA), gibberellin-regulated protein 9 (GAS9), auxin-induced protein AUX28, abscisic acid 8'-hydroxylase (CYP707A), auxin-responsive protein SAUR72, abscisic acid receptor PYR2, cytokinin hydroxylase-like | MYB, bHLH, AUX/IAA, AP2, AP2/ERF, SBP, CAAT, HSF, MBF1, bZIP, NAC, MADS, GRF, WRKY |

(Continued)
| Table 3. Continued |  |
|---|---|---|---|---|---|---|
| **Cucurbitaceae** | **Color-related genes** | **Texture-related genes** | **Aroma-, flavor-, and taste-related genes** | **Plant hormone-related genes** | **Key transcription factors** |
| Pumpkin (Cucurbita maxima) | phytoene synthase (PSY), 15-cis-phytoene desaturase (PDS), zeta-carotene desaturase (ZISO), polypropylene isomerase (CRTISO), lycopene epsilon cyclase (LCYE), lycopene beta-cyclase (LCYB), beta-ring hydrolase (CYP97A3), beta-carotene 3-hydroxylase (BCH), carotene epsilon monooxygenase (CYP97C1), zeaxanthin epoxide (ZEP), violaxanthin de-epoxidase (VDE), chalcone synthase (CHS) | endoglucanase (EG), expansin (EXP), xylanoglucan endotransglycosylase/hydrolase protein (XTH), beta-amylase 1 (BMY1), pectate lyase-like (PL), pectin acetyltransferase (Pect), beta-galactosidase (beta-Gal), beta-galacturonase (PG), glucan endo-1,3-beta-glucosidase (BG), cellulose synthase (CESA) | alcohol dehydrogenase (ADH), beta-fructofuranosidase (INV), fructokinase (FK), hexokinase (HK), glucose-6-phosphate isomerase (PGI), phosphoglucomutase (PGM), UTP-glucose-1-phosphate uridylyltransferase (UGPase), sucrose synthase (SUS), sucrose-phosphate synthase (SPS), ADP-sugar diphosphatase (Nudix14), glucose-1-phosphate dehydrogenase (AGPase), 1,4-alpha-glucan branching enzyme (SBE), trehalose 6-phosphate synthase/phosphatase (TPS), alpha-amylase (alpha-A), 4-alpha-glucanotransferase (malQ), UDP-glucose 6-dehydrogenase (UGDH), UDP-glucose 6-dehydrogenase (UDG), UDP-glucose decarboxylase (UXS1), 1,4-beta-D-xylan synthase (XS), beta-D-xylan synthase 4 (XYL4), UDP-glucose 4-epimerase (GAE), alpha-1,4-galacturonosyltransferase (GALT) | 1-aminoacyclopentane-1-carboxylate oxidase (ACO), 1-aminoacyclopropene-1-carboxylate synthase (ACS), ethylene insensitive 2/3 (EIN2/3), ethylene-responsive transcription factor (ERF), ethylene receptor 1 (ETR1), ethylene response sensor 1 (ERS1), gibberellin 2-oxidase (GA2ox), gibberellin 2-oxidase (GA2ox), auxin-induced protein, auxin response factor 6 (ARF6), auxin-responsive protein IAA (IAA), gibberellin-regulated protein (GASA), abscisic acid 8'-hydroxylase (CYP707A) | bHLH, AP2/ERF, MYB, NAC, AUX/IAA, bZIP, WRKY |
| Snake gourd (Trigynopsis aurea) | phytoene synthase (PSY), 15-cis-phytoene desaturase (PDS), polypropylene isomerase (CRTISO), zeta-carotene desaturase (ZDS), lycopene beta-cyclase (LCYB), lycopene epsilon cyclase (LCYE), 15-cis-zeta-carotene isomerase (ZISO), 9-cis-epoxycarotenoid dioxygenase NCED2 (NCED2), beta-carotene 3-hydroxylase 1 (BCH1), carotene epsilon monooxygenase (CYP97C1) | cellulase synthase-like protein E (CSLE1), endoglucanase (EG), expansin (EXP), glucan 1,3-beta-glucosidase (BGL), pectinesterase (PE), polygalacturonase (PG), beta-galactosidase (beta-Gal), glucan endo-1,3-beta-glucosidase (BGL2), pectin acetyltransferase (Pect), pectin methyltransferase (PMT), beta-glucosidase (beta-Glu), pectate lyase (PL), glucan endo-1,3-beta-glucosidase (BG) | linolate 95-lipoxygenase-like (LOX), linolate 135-lipoxygenase 2-1 (LOX), alkohol dehydrogenase (ADH), glutamate dehydrogenase 1 (GDH1), phenylalanine ammonia-lyase (PAL), sucrose synthase (SUS) | 1-aminoacylcyclopentane-1-carboxylate oxidase (ACO), ethylene-responsive transcription factor (ERF), ethylene receptor 2 (ETR2), abscisic acid receptor PYRI-like, auxin-induced protein, auxin-responsive protein IAA, auxin-responsive protein factor (ARF), abscisic acid receptor PYRI, auxin-responsive protein SAUR50-like, gibberellin-regulated protein (GASA), gibberellin receptor, abscisic acid 8'-hydroxylase 4-like, gibberellin 2-beta-dioxygenase 1-like, gibberellin 3-oxidase 3 (GA3ox3), auxin transporter-like protein (LAX), auxin-responsive protein SAUR71-like, ethylene insensitive 3 (EIN3), ethylene response sensor 1 (ERS1) | AP2/ERF, MYC, ERF, ANT |

(Continued)
| Cucurbitaceae | Color-related genes | Texture-related genes | Aroma-, flavor-, and taste-related genes | Plant hormone-related genes | Key transcription factors |
|--------------|---------------------|-----------------------|-----------------------------------------|-----------------------------|--------------------------|
| Chayote (Sechium edule) | phytoene synthase (PSY), 9-cis-epoxycarotenoid dioxygenase NCED2/3 (NCED2/3), zeaxanthin epoxidase (ZEP), carotenoid 9,10-dehydroxydrase (CCD1), carotenoid cleavage dioxygenase 4/8 (CCD4/8), β-carotene hydroxylase 2 (BCH2), β-carotene isomerase D27 (D27), flavonol synthase (FLS), chalcone synthase 2 (CHS2) | expansin (EXP), glucan endo-1,3-β-glucosidase (BG), polygalacturonase (PG), xyloglucan endotransglycosylase/hydrolase (XTH), β-galactosidase (β-Gal), α-glucosidase (β-Glu), cellulase synthase (CesA), endoglucanase (EG), pectin acetylxyluronase (PM), pectinesterase (PE), α-mannosidase (MANA), β-amylase 1 (BMY1), pectin methylesterase (Pme), pectinesterase/pectinesterase inhibitor 25 (PME25), pectate lyase (PL) | linoleate 13S-lipoxygenase 2-1 (LOX), linoleate 13S-lipoxygenase 3-1 (LOX), linoleate 9S-lipoxygenase (LOX), alcohol dehydrogenase-like 6 (ADH6), glutamate dehydrogenase 2 (GDH2), terpene synthase 10 (TPS10), sucrose-phosphate synthase 1 (SPS1), sucrose synthase (SUS), sucrose-phosphatase 1 (SPP1) | 1-aminocyclopropane-1-carboxylate synthase (ACS), 1-aminocyclopropane-1-carboxylate oxidase (ACO), ethylene-responsive transcription factor (ERF), abscisic acid 8-hydroxylase (CYP707A), auxin response factor (ARF), auxin-induced protein, auxin-responsive protein IAA, gibberellin receptor GID1B, abscisic acid receptor PYL8/9, auxin-responsive protein SAUR, gibberellin 20 oxidase 1 (GA20ox1), gibberellin 2-β-dioxygenase (GA20x), gibberellin-regulated protein 14 (GASA14) | AP2, MYB, NAC, WRKY, MYC, bHLH, SBP, AP2/ERF, bZIP, GRF |
resequenced 20 watermelon accessions and identified many disease-resistance genes that had been lost during domestication. Thus, improving resistance to pathogens is an ongoing goal of sweet watermelon breeding programs. Interestingly, Cucurbita amarus, Cucurbitus colocynthis, and Citrullus mucosospermus have been used for breeding studies to find new sources of disease and insect resistance to improve sweet watermelon. Whole-genome resequencing of 414 accessions identified genomic regions associated with critical fruit quality traits and using GWAS identified a total of 43 association signals, which provided useful information for watermelon breeding [32].

Bitter gourd is an important vegetable and medicinal plant in the Cucurbitaceae family. The bitter taste of bitter gourd is due to the existence of cucurbit triterpenoid compounds cucurbitacins [42] and it has the potential for further improvement [41]. A total of 1507 marker loci were genotyped by using restriction-associated DNA tag sequencing (RAD-seq) analysis, resulting in an improved linkage map [6]. A total of 255 scaffolds were assigned to the linkage map through anchoring RAD tag markers [6]. Interspecific crosses play a vital part in Cucurbita breeding for transferring favorable traits between species [34], and 40 transcriptomes assembled for 11 species of Cucurbitaceae plants have a significant development potential for obtaining new cucurbit phenotypes with ideal traits. A reverse genetic approach, Targeting Induced Local Lesions in Genomes (TILLING), can be applied to the breeding of Cucurbitaceae crops and help to improve agronomic traits [226]. Different DNA mutant TILLING libraries have been set up in cucurbits [227–231]. This approach has provided a resource for plant breeding programs and future functional genomics study. Genome editing technology is attracting attention and breeding efficiency can be rapidly improved through combining the genomic and variomic information on crops [232]. Developing efficient and reliable genetic transformation technology for the target crops will contribute to the wide application of this approach in Cucurbitaceae crops. CRISPR/Cas9 is a common and efficient technique for genome editing and has been used for Cucurbitaceae crops to knock out target genes and obtain crop materials with desirable agronomic traits [233, 234], such as cucumber [235, 236], watermelon [237, 238], and pumpkin [239], and has become a precision-breeding approach for modifying traits in plants species [240]. In the future, a wide range of genome analysis and editing research is expected to expand our understanding and implementation for Cucurbitaceae plant breeding programs.

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Conflict of interests
The authors declare that they have no conflict of interests.

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