Chloroplasts arose more than 1 billion years ago, when a free-living cyanobacterium became an endosymbiont in a eukaryotic host cell. Several lines of evidence indicate that all chloroplasts and their nonphotosynthetic relatives (plastids) are directly or indirectly derived from a single endosymbiotic event (Reyes-Prieto et al., 2007; Gould et al., 2008; Archibald, 2009; Fig. 1). The original endosymbiosis of the cyanobacterium gave rise to plastids (primary plastids) in the Archaeplastida, which are made up of the Glauco phyra, Rhodophyta (red algae), and Viridiplantae (green algae and land plants). All other plastids, such as those found in kelps, dinoflagellates, malaria parasites (these three belong to the Chromalveolata), Euglenids (Excavata), and chlorarachniophytes (Rhizaria), were established by subsequent endosymbiotic events in which eukaryotic algae had become integrated into other eukaryotes. Recent phylogenetic studies have classified eukaryotes into six supergroups: Amoebozoa, Opisthokonta (fungi and animals), Archaeplastida, Chromalveolata, Excavata, and Rhizaria. Thus, four of the six eukaryotic supergroups possess plastids (Reyes-Prieto et al., 2007; Gould et al., 2008; Archibald, 2009; Fig. 1).

The conversion of a cyanobacterium to plastids required several steps (Reyes-Prieto et al., 2007; Gould et al., 2008; Archibald, 2009). Theoretically, a specific relationship developed between an endosymbiont and host, such as a predator-prey relationship. Subsequently, mechanisms controlling metabolic exchange between the two developed. Most of the genes that were once in the endosymbiont genome were either lost or transferred into the host nuclear genome. As a result, the size of the plastid genome has been reduced to less than one-tenth that of the free-living cyanobacterial genome. Thus, the bulk of the plastid proteome consists of nucleus-encoded proteins that are translated on the plastid or just a few plastids. Thus, chloroplast division is synchronized with the host cell cycle such that the chloroplast divides before cytokinesis and is thus transmitted into each daughter cell.

The requirement of division synchronization is supported by several other endosymbiotic relationships. For example, certain species of heterotrophic dinoflagellates engulf eukaryotic algae and use them as temporary plastids (called “kleptoplasts”) for a period of days to weeks before digesting them. In contrast, a few dinoflagellate species maintain a eukaryotic algal unci cell (i.e. containing the nucleus, mitochondria, Golgi apparatuses, etc.) as a permanent endosymbiont by synchronizing the endosymbiont cell division to the host cell cycle (Wouters et al., 2009; Imanian et al., 2010). A similar situation is also observed in other eukaryotic groups. Hatera arenicola has a transient green algal endosymbiont, and this photosynthetic endosymbiont is inherited by only one daughter cell during cell division. Daughter cells that have lost the endosymbiont again engulf the green alga (Okamoto and Inouye, 2005). H. arenicola (Katablepharidophyta) bears a close evolutionary relationship with cryptophytes, in which permanent plastids of a red algal origin have been established by division synchronization (Fig. 1). There are also eukaryotes that possess permanent cyanobacterial endosymbionts, such as Paulinella chloroplastophora. This endosymbiont is consistently inherited by progeny cells as a consequence of tight synchronization of host and endosymbiotic cell cycles (Melkonian and Mollenhauer, 2005).

Currently, it is largely unknown how endosymbiotic cell division is regulated by host cells in the diverse array of endosymbiotic relationships. However, studies over the last decade have rapidly provided information on the mechanism and the regulation of primary chloroplast division (Kuroiwa et al., 2008; Yang et al., 2008; Maple and Møller, 2010; Miyagishima and Kabeya, 2010; Pyke, 2010). In addition, several genome projects on the plastid-carrying eukaryotes have been initiated. These advances promise the eventual understanding of the mechanisms that coordinate the proliferation of both a host cell and an endosymbiont.

The mechanism of primary plastid division, especially that of plastids, has been summarized in...
recent reviews (Kuroiwa et al., 2008; Yang et al., 2008; Maple and Møller, 2010; Miyagishima and Kabeya, 2010; Pyke, 2010). Here, the mechanism of primary chloroplast division is briefly introduced, and then the common and diverse mechanisms underlying division in other types of plastids and photosynthetic endosymbionts will be discussed. Note that, in this review, the term “chloroplasts” is used to indicate photosynthetic plastids.

Figure 1. A schematic view of the origin and spread of plastids in the putative six eukaryotic supergroups (modified from Archibald, 2009). The broken lines denote uncertainty of branch positions in the tree. Red algae and groups containing plastids of red algal origin are shown in red. Viridiplanetae (green algae and land plants) and groups containing plastids of green algal origin are shown in green. Arrows indicate the primary endosymbiotic event of a cyanobacterium (1st) and secondary endosymbiotic events (2nd). The position of secondary endosymbiotic events in the tree is still uncertain at present. Note that some dinoflagellates possess plastids of stramenopile, haptophyte, or green algal origin, although those are not indicted in the scheme. It is suggested that these dinoflagellates replaced the original red algal chloroplast with chloroplasts of other origin by another endosymbiotic event (Gould et al., 2008).

PRIMARY CHLOROPLAST DIVISION BY DIVISION COMPLEX OF CHIMERIC ORIGIN

Chloroplasts usually divide by binary fission (Fig. 2), but multiple fission also occurs in certain cases (Duckett and Ligrone, 1993). Earlier electron microscopic studies established that chloroplast division is performed by the simultaneous constriction of the inner and outer envelopes at the division site. Since the 1980s, electron-dense ring structures at the division site called plastid-dividing (PD) rings have been detected on both the inside and outside of the chloroplast, suggesting that chloroplast division is performed by constriction of the ring-like division complex (Kuroiwa et al., 1998).

Recent studies, especially molecular genetic studies on leaf chloroplasts in Arabidopsis (Arabidopsis thaliana) and chloroplasts in the unicellular red alga Cyanidioschyzon merolae, have identified several components of the division complex. As observed by electron microscopy, the division complex encompasses both the inside and the outside of the two envelopes (Fig. 2). All of the known components are encoded in the host nuclear genome, except for a few components of cyanobacterial origin encoded in the chloroplast genome in certain algal lineages (Kuroiwa et al., 2008; Yang et al., 2008; Maple and Møller, 2010; Miyagishima and Kabeya, 2010; Pyke, 2010).

Components Descended from the Cyanobacterial Endosymbiont

Consistent with the endosymbiotic origin of plastids, the stromal portion of the chloroplast division complex is descended from the cyanobacterial cell division machinery (Figs. 2 and 3; Table I). As in bacteria, Filamenting temperature-sensitive mutant Z (FtsZ; a prokaryotic tubulin-like GTPase) self-assembles into a ring structure on the stromal side of the chloroplast division site and is involved in the division process (Osteryoung and Vierling, 1995; Osteryoung et al., 1998; Strepp et al., 1998; Mori et al., 2001; Vitha et al., 2001). In addition to FtsZ, certain other components, such as ACCUMULATION AND REPLICA- TION OF CHLOROPLAST 6 (ARC6; an ortholog of cyanobacterial division protein Ftn2; Vitha et al., 2003), are also descended from the cyanobacterial division machinery. However, many other components were lost after the endosymbiotic event (Figs. 2 and 3).

Although plastids have retained some of the cyanobacterial division machinery, both duplication and differentiation of the cyanobacteria-descended components have played significant roles in the evolution of the plastid division machinery (Figs. 2 and 3; Table I). While cyanobacterial genomes encode a single FtsZ protein, two phylogenetically and functionally distinct
FtsZ proteins evolved in algae and plants by gene duplication and differentiation (Osteryoung et al., 1998; Osteryoung and McAndrew, 2001; Stokes and Osteryoung, 2003; Miyagishima et al., 2004). Both proteins colocalize on the stromal side of the division site (McAndrew et al., 2001; Kuroiwa et al., 2002). FtsZ2 in Viridiplantae has retained a short C-terminal domain (Osteryoung and McAndrew, 2001) that is essential for binding to the inner envelope-spanning protein ARC6 (Maple et al., 2005). In contrast, FtsZ1 lacks the C-terminal motif and does not interact with ARC6 (Maple et al., 2005) but interacts with ARC3 (Maple et al., 2007), a chloroplast division protein unique to Viridiplantae (Shimada et al., 2004). ARC3 also evolved by modification of FtsZ. It consists of an incomplete FtsZ-like domain and the MORN motif, which is known to bind to membrane lipids in other proteins. The duplication of the FtsZ protein and subsequent loss of the C-terminal domain also occurred in red algae and in stramenopiles after the secondary endosymbiotic event, independently from the event that occurred in Viridiplantae (Miyagishima et al., 2004).
Components Derived from the Host Cell

In addition to the modification of cyanobacteria-descended proteins, some components of eukaryotic host origin have become integrated into the chloroplast division machinery (Figs. 2 and 3; Table II). DRP5B (ARC5) is a member of the eukaryotic dynamin family of GTPases and localizes on the cytosolic side of the chloroplast division complex (Gao et al., 2003; Miyagishima et al., 2003). Proteins of this family form helical assemblies on the membrane, and it is suggested that constriction and disassembly of the helix result in membrane fission (Roux and Antonny, 2008). Phylogenetically, DRP5B is most closely related to DRP5A protein. DRP5A is not involved in plastid division (Gao, 2005) but rather is involved in cytokinesis in Arabidopsis and the slime mold Dictyostelium discoideum (Miyagishima et al., 2008). Thus, the dynamin in chloroplast division probably evolved from the cytokinetic activity of the eukaryotic host cell. PDV1 and PDV2 are unique to land plants and are required for the recruitment of DRP5B (Miyagishima et al., 2006). It appears that PDV proteins connect the cyanobacteria-descended stromal complex and the host-derived cytolytic complex (Glynn et al., 2008, 2009; Figs. 2 and 3). However, it is not known whether PDV proteins directly interact with DRP5B or how the two complexes are connected in algae, which do not have PDV proteins.

The PD ring has been detected by electron microscopy in several different lineages of algae and land plants to usually have two structures: the outer PD ring on the cytosolic side of the outer envelope, and the inner PD ring on the stromal side of the inner envelope (Kuroiwa et al., 1998). Occasionally, a middle

Table 1. Cyanobacteria-derived components of the chloroplast division machinery

<table>
<thead>
<tr>
<th>Component (Localization)</th>
<th>Function and Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>FtsZ1/FtsZ2 (medial ring)</td>
<td>Nucleus-encoded FtsZ proteins are required for normal chloroplast division. In bacteria, the FtsZ ring acts as the scaffold for recruitment of other key cell division proteins. Bacterial FtsZ self-assembles into a ring that constrains liposomes in vitro, suggesting that the FtsZ ring generates constrictive force in vivo. Green algae and land plants have two types of phylogenetically distinct nucleus-encoded FtsZ proteins. FtsZ1 emerged by duplication of the FtsZ2 protein after the endosymbiotic event. Unlike FtsZ2 and cyanobacterial FtsZ, FtsZ1 does not contain a short C-terminal motif. The C-terminal motif mediates the interaction between FtsZ2 and ARC6.</td>
</tr>
<tr>
<td>ARC6/PARC6 (medial ring/medial ring and poles)</td>
<td>Nucleus-encoded ARC6 and PARC6 (a paralog of ARC6 unique to vascular plants) are required for normal chloroplast division. Both proteins are descended from Ftn2 (ZipN), which is a component of the cyanobacterial division complex. ARC6 promotes FtsZ assembly through direct interaction with FtsZ2, while PARC6 destabilizes the FtsZ polymer, most likely via direct interaction with ARC3. ARC6 recruits PDV2 through direct interaction with PDV2 in the intermembrane space, while PARC6 is required for the recruitment of PDV1 (it is unknown whether PARC6 and PDV1 directly interact).</td>
</tr>
<tr>
<td>SepF (medial ring?)</td>
<td>SepF is encoded in the plastid (cyanelle) genome of the glaucophyte C. paradoxa, but the function in plastid division has not been determined. In bacteria, SepF is required for normal cell division. SepF localizes at the division site by interaction with FtsZ.</td>
</tr>
<tr>
<td>FtsW (medial ring!)</td>
<td>FtsW is encoded in the plastid genome of glaucophytes and a certain green algae, but the function is unknown. In bacteria, FtsW spans the cytoplasmic membrane at the division site and recruits FtsI.</td>
</tr>
<tr>
<td>FtsI (medial ring?)</td>
<td>FtsI is encoded in the plastid genome of a certain green algae, but the function has not been determined. FtsI spans the cytoplasmic membrane at the division site and its periplasmic domain that cross-links the newly synthesized peptidoglycan strand.</td>
</tr>
<tr>
<td>MinC (unknown)</td>
<td>MinC is encoded in the nuclear genome of (some) certain algal lineages and the moss P. patens, but the function has not been determined. In bacteria, MinC, MinD, MinE (proteobacteria), and DivIV/A (firmicutes) determine the site of FtsZ ring formation. MinC inhibits FtsZ polymerization.</td>
</tr>
<tr>
<td>MinD (medial ring and punctate structures)</td>
<td>MinD is a membrane-associated ATPase. The nucleus-encoded MinD protein regulates positioning of the chloroplast FtsZ ring. In bacteria, MinD localizes MinC to the cytoplasmic membrane by direct interaction with MinC.</td>
</tr>
<tr>
<td>MinE (unknown)</td>
<td>The nucleus-encoded MinE protein regulates the positioning of the chloroplast FtsZ ring. In proteobacteria, MinE restricts the inhibitory activity of the MinCD complex to the cell pole, thereby allowing the FtsZ ring to form at the midcell position. MinE stimulates ATP hydrolysis of MinD, which releases the MinCD complex from the cytoplasmic membrane.</td>
</tr>
</tbody>
</table>

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The outer PD ring is observed in the intermembrane space (Miyagishima et al., 2001; Sumiya et al., 2008). A very recent study that was performed by dissecting the plastid division complex in the red alga *C. merolae* showed that the outer PD ring is a bundle of polyglucan filaments (Yoshida et al., 2010). These filaments are associated with the PDR1 protein, which is most closely related to the eukaryotic glycogenin proteins. Because glycogenin proteins are known to polymerize Glc, PDR1 likely synthesizes the polyglucan filaments of the PD ring. The filaments of the outer PD ring have been observed in several different lineages (Kuroiwa et al., 1998), and potential orthologs of PDR1 are encoded in land plant genomes (Yoshida et al., 2010). However, the genomes of other plastid-carrying eukaryotes, such as green algae and stramenopiles, apparently lack the PDR1 gene; thus, how the filament is synthesized is uncertain at present.

**Division Site Selection**

Chloroplasts normally divide at the midpoint, yielding two daughter chloroplasts of equal size (Fig. 2). The mechanism responsible for the positioning of the FtsZ ring is also descended from the cyanobacterial machinery known as the Min system (Figs. 2 and 3; Table I). The cyanobacterial Min system involves MinC, MinD, MinE, and probably Cdv3 (DivIVA-like) proteins (Mazouni et al., 2004; Miyagishima et al., 2005; Marbouty et al., 2009). In bacteria, MinC is an inhibitor of FtsZ polymerization and forms a complex with MinD, MinE in *Escherichia coli* (a gram-negative proteobacterium) and DivIVA in *Bacillus subtilis* (a gram-positive firmicute) regulate the positioning of MinCD such that the FtsZ ring forms only at the midcell position (Harry et al., 2006). The mechanism of the division site selection has also been modified since the endosymbiotic event (Figs. 2 and 3; Tables I and II). MinC and Cdv3 have been lost, although certain algal lineages and the moss *Physcomitrella patens* still possess a MinC-like protein (Yang et al., 2008; Miyagishima and Kabeya, 2010). A recent study suggests that ARC3 fulfills the function of MinC in Viridiplantae (Maple et al., 2007). Overexpression of ARC3 inhibits chloroplast division, most likely through an inhibition of the FtsZ assembly, like the case of bacterial MinC. ARC3 interacts with MinD, MinE, FtsZ1 (Maple et al., 2007), and PARC6 (Glynn et al., 2009). The *arc3* mutant exhibits multiple FtsZ rings within a single enlarged chloroplast, similar to the Arabidopsis *minD* mutant and bacterial *minC* and *minD* mutants (Glynn et al., 2007). MULTIPLE CHLOROPLAST DIVISION SITE 1 (MCD1), a protein unique to land plants, is also involved in the positioning of the plastid FtsZ ring. MCD1 recruits MinD to the proper location, and the *mcd1* mutant exhibits multiple FtsZ rings in a single chloroplast (Nakanishi et al., 2009). The Min system is widely conserved in algae and land
plants, but the genome of the red alga C. merolae does not encode any of the proteins described above. Currently, it is not known how the FtsZ ring is positioned at the midpoint in this organism.

**Formation and Constriction of the Chloroplast Division Machinery**

Studies in Arabidopsis (Miyagishima et al., 2006; Glynn et al., 2008, 2009) and C. merolae (Miyagishima et al., 2003; Yoshida et al., 2010) suggest that the plastid division complex is assembled from the inside to the outside of the chloroplast before the onset of division site constriction, in the order of the FtsZ ring, inner PD ring, outer PD ring, and DRP5B ring (Miyagishima et al., 2003, 2006; Glynn et al., 2008, 2009; Yoshida et al., 2010; Fig. 2). Thus, topological information is conveyed from the stromal complex that is descended from the cyanobacterial endosymbiont to the cytosolic complex of host eukaryotic origin.

Currently, how the division complex constricts the two envelopes is essentially a matter of speculation. Bacterial FtsZ self-assembles into rings inside of liposomes and induces constrictions of these liposomes in vitro (Osawa et al., 2008). The helical self-assembly of dynamin tabulates liposomes, and disassembly of the helix results in membrane fission in vitro (Roux and Antonny, 2008). Thus, FtsZ and DRP5B probably participate in the generation of constrictive force in plastid division. However, there is a certain time lag between FtsZ ring formation and the onset of plastid division site constriction. Constriction starts after the other components of the division complex have been assembled in the division complex (Miyagishima et al., 2003). A similar time lag has been observed in bacterial cell division (Aarsman et al., 2005; Gamba et al., 2009).

It is proposed that the sliding of the PD ring filaments mediated by DRP5B likely produces the constrictive force (Yoshida et al., 2006), but such sliding of the filaments has not been demonstrated. DRP5B forms punctate rings (Gao et al., 2003; Miyagishima et al., 2003), unlike other components of the division complex, which have been observed to form continuous rings by fluorescence microscopy. In Arabidopsis, the enlarged chloroplasts in *drp5B (arc5)* (Pyke and Leech, 1994) or *pdr* (Miyagishima et al., 2006) mutants can still divide by constriction (note that DRP5A, which is most closely related to DRP5B, is not involved in plastid division as described above). Future functional studies in vivo and in vitro at a higher resolution will ultimately shed light on how the division complex constricts double-membraned plastids.

**PLASTID DIFFERENTIATION AND PLASTID DIVISION**

In algae and mosses, chloroplasts are usually the only type of plastid present. This is consistent with the fact that the vegetative cells of cyanobacteria remain blue-green and photosynthetic throughout their life cycle. Thus, from an evolutionary standpoint, the chloroplast is the origin of plastids.

Vascular plants have evolved a complex plastid differentiation system in which all of the plastids, such as chloroplasts, chromoplasts, leucoplasts, and amylloplasts, are derived from nongreen proplastids in meristematic cells (Lopez-Juez and Pyke, 2005). For example, in spinach (*Spinacia oleracea*), the shoot apical meristem contains approximately 12 proplastids, the division of which keeps pace with cell division so that newly formed cells have essentially the same number of proplastids. During leaf development, cells expand without cell division (but with endoreduplication), yet the chloroplasts still continue to divide and the number of chloroplasts per cell eventually reaches approximately 200 (Possingham and Lawrence, 1983).

Previous microscopic studies showed that all types of plastids are capable of division (Possingham and Lawrence, 1983). However, in spite of recent remarkable advances in understanding the mechanism of chloroplast division, few studies have addressed the mechanism governing the division of the nongreen plastids (Pyke, 2010). This is largely because nongreen plastids are smaller than chloroplasts and observation requires fluorescent staining or electron microscopy. In addition, some plastids exhibit irregular shapes with numerous tubular connections between them called stromules (Hanson and Sattarzadeh, 2008). In some cases, multiple FtsZ rings form in a single plastid, and multiple fission has been observed (Momoyama et al., 2003; Yun and Kawagoe, 2009; Pyke, 2010).

Observation of nongreen plastids in chloroplast division mutants and analyses of the localization of the chloroplast division proteins have shown that nongreen plastid division utilizes division machinery similar to that in chloroplasts (Table III). However, these investigations have also revealed certain differences between chloroplasts and the nongreen plastids (Table III). For example, there is no detectable defect in proplastid division in the *drp5b (arc5)* mutant (Roberson et al., 1996; Pyke, 1999), and the DRP5B protein is not detected in the shoot apical meristem (Okazaki et al., 2009). Thus, land plants apparently have evolved a plastid division mechanism that does not require DRP5B protein.

In addition, there might be a plastid division mechanism that does not utilize the known plastid division complex. Whereas the *arc6* mutation impairs FtsZ assembly (Vitha et al., 2003) and results in severe defects in both chloroplast and proplastid division (Robertson et al., 1995; Pyke, 1999), the photosynthetic cells in *arc6* contain irregularly shaped nongreen plastids along with chloroplasts. These abnormal plastids somehow proliferate in the *arc6* mutant (Chen et al., 2009). A similar type of plastid proliferation also occurs in a tomato (*Solanum lycopersicum*) chloroplast division mutant, where budding and fragmentation of the plastids are observed (Forth and Pyke, 2006). A very recent study showed that Arabidopsis mutants in which FtsZ proteins are completely depleted are
Other Proteins Related to Plastid Division

Proteins other than the ones described above have also been implicated in plastid division in Arabidopsis. When the GIANT CHLOROPLAST 1 (GC1; also called AtSulA; Maple et al., 2004; Raynaud et al., 2004), CRUMPLED LEAF (CRL; Asano et al., 2004), Msc-like genes ([MSL]; and MSL3; Haswell and Meyerowitz, 2006), AtCDT1 (Raynaud et al., 2005), or CPN60 (Suzuki et al., 2009) gene is inactivated, plastid division is impaired and giant plastids are generated, as in other bona fide plastid division genes. At present, it is not known whether these proteins are directly involved in chloroplast division machinery or how these proteins are related to plastid division.

CRL (Asano et al., 2004) and GC1 (Maple et al., 2004; Raynaud et al., 2004) are descended from the cyanobacterial endosymbiont. Some of the bacterial orthologs of GC1 are annotated as SulA-like proteins. SulA functions as an inhibitor of FtsZ assembly in E. coli (Harry et al., 2006; de Boer, 2010). However, there is no evident similarity between GC1 and E. coli SulA at the level of primary structure and no experimental evidence that GC1 is a functional counterpart of SulA. MSL proteins are homologs of bacterial mechanosensitive ion channels and likely control plastid size and shape (Haswell and Meyerowitz, 2006). AtCDT1 (for Cdc10-dependent transcript 1) are dually targeted to both the nucleus and plastids and likely coordinate the cell cycle as well as plastid division (Raynaud et al., 2005).

SECONDARY PLASTID DIVISION

A diverse array of eukaryotic lineages possess plastids (most are chloroplasts) that are of secondary endosymbiotic origin (Fig. 1). In addition, plastids of tertiary endosymbiotic origin have been found in certain species of dinoflagellates. The secondary endosymbiosis of a red algal ancestor gave rise to plastids in Chromalveolata, such as stramenopiles, haptophytes, cryptophytes, most of the photosynthetic dinoflagellates, and apicomplexan parasites. Euglenids and chlorarachniophytes possess chloroplasts of a green algal origin. The question of exactly how many endosymbiotic events have given rise to this evident diversity remains elusive. However, several reports have indicated a preference for the hypothesis that the red algal endosymbiosis and subsequent reduction into chloroplasts occurred only once in the common ancestor of chromalveolates (Reyes-Prieto et al., 2007; Gould et al., 2008; Archibald, 2009). This scenario also suggests that several chromalveolate lineages, such as ciliates, oomycetes, and plastid-lacking lineages of dinoflagellates, have subsequently lost the plastids.

Little is known about how secondary plastids in the diverse eukaryotic lineages divide, but a few studies of stramenopile chloroplast division and recent genome projects of Chromista (stramenopiles, haptophytes, and cryptophytes) suggest that a part of the chloroplast division machinery in these lineages is descended from a red algal endosymbiont (Fig. 4). The chloroplasts in Chromista are surrounded by four membranes. The inner two membranes are descended from the inner and

Table III. Involvement of chloroplast division proteins in proplastid division in the shoot or root apical meristem

<table>
<thead>
<tr>
<th>Components</th>
<th>Localization</th>
<th>Meristematic Proplastid Division in Mutants</th>
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<tbody>
<tr>
<td>FtsZ1/FtsZ2</td>
<td>Midplastid ring</td>
<td>Division defect</td>
</tr>
<tr>
<td>ARC6/ParC6</td>
<td>Midplastid ring</td>
<td>Division defect (arc6); n/d (parc6)</td>
</tr>
<tr>
<td>IniE</td>
<td>n/d</td>
<td>Division defect</td>
</tr>
<tr>
<td>PDV1/PDV2</td>
<td>Midplastid ring</td>
<td>Division defect</td>
</tr>
<tr>
<td>DRP5B</td>
<td>Not detected</td>
<td>Slight difference from the wild type</td>
</tr>
<tr>
<td>Outer PD ring</td>
<td>Midplastid ring</td>
<td>n/d</td>
</tr>
<tr>
<td>Inner PD ring</td>
<td>Midplastid ring</td>
<td>n/d</td>
</tr>
</tbody>
</table>

the outer envelopes of the primary chloroplast. The two additional membranes are thought to correspond to the plasma membrane of the engulfed alga and the phagosomal membrane of the host cell, respectively (Fig. 4). Currently, it is not known how the outer pair of membranes divides, but observations of stramenopile species suggest that the division is carried out by a mechanism that is distinct from the primary chloroplast division. In certain lineages, the outer pair of membranes divides in the same plane as the inner pair, but the constriction of the outer pair takes place behind that of the inner pair. In addition, spherical vesicles have been observed in the space between the two pairs of membranes (called the periplastid compartment) at the division site (Hashimoto, 1998, 2005). In rare cases, such as in Synchronia, the division of the inner and the outer pair is not coupled. Thus, a number of chloroplasts with two inner membranes share a single outer pair of membranes (Horn et al., 2007).

Apicomplexans, such as malaria parasites (Plasmodium), also possess four-membrane-bound nonphotosynthetic plasts (called apicoplasts). In this group, the plastid division involves simultaneous constriction of the four membranes. In contrast to Chromista, apicomplexan genomes do not encode any of the known primary plastid division proteins. A recent study in the apicomplexan Toxoplasma gondii showed that the dynamin-like protein TgDRPA localizes on the cytosolic side of the apicoplast division site (i.e. on the outermost membrane), where it is required for the apicoplast division (van Dooren et al., 2009; Fig. 4). DRPA is well conserved in but unique to the apicomplexans (i.e. DRPA is not a descendant of the DRP5B in the primary chloroplast division; van Dooren et al., 2009). Thus, apicomplexans have probably lost the primary chloroplast division machinery and have developed new mechanisms for division. It is not known how this transition occurred or whether the loss of the primary chloroplast division machinery is related to the loss of photosynthetic activity. Studies of chloroplast division in photosynthetic relatives of apicomplexans, such as Chromera (Moore et al., 2008; Fig. 1), would be expected to shed light on this issue.

**REGULATION OF PLASTID DIVISION**

Many unicellular and multicellular algae have either one or just a few chloroplasts per cell. Thus, chloroplasts divide during a specific stage of the host cell cycle before the host cell completes cytokinesis (Fig. 5). Studies in red algae (Takahara et al., 2000; Fujiwara et al., 2009), a green alga (Adams et al., 2008), and a stramenopile (Gillard et al., 2008) suggest that the regulation of algal chloroplast division partly relies on the cell cycle-based expression of the chloroplast division genes.

In contrast, land plant cells generally contain dozens of plastids, except that hornwort (Anthocerotophyta) cells contain a single chloroplast or a few chloroplasts.
In the shoot apical meristem, there likely is a correlation between cell cycle progression and plastid division (Seguí-Simarro and Staehelin, 2009), whereas plastids generally divide nonsynchronously, even in the same cell (e.g. chloroplasts in the moss *P. patens*; Fig. 2). Moreover, the plastid division rate changes in accord with cell differentiation, resulting in changes of plastid size and number (Fig. 5). Many earlier studies have indicated that various environmental stimuli impact the chloroplast division rate (Possingham and Lawrence, 1983; Lopez-Juez and Pyke, 2005). Currently, it is largely unknown how plastid division is regulated in land plants, but a recent study showed that PDV proteins determine the rate of plastid division in land plants (Okazaki et al., 2009). The level of PDV proteins in the division complex changes during cell differentiation, where either an increase or a decrease of the PDV1 and PDV2 levels results in a corresponding increase or decrease in the plastid division rate. For example, the PDV level is highest in the proximity of the shoot apical meristem. The level of PDV proteins, but not other components of the division complex, decreases during leaf development, resulting in a decrease of the chloroplast division rate and an increase in chloroplast size. It is not currently known how PDV proteins regulate the chloroplast division rate, but it appears that PDV proteins regulate the rate of division site constriction (Okazaki et al., 2009).

CHLOROPLASTS IN GLAUCOPHYTES AND INTERMEDIATES BETWEEN CYANOBACTERIA AND PLASTIDS

Unlike plastids in other organisms, the chloroplasts of glaucophyte algae (called cyanelles) have retained a peptidoglycan layer between the two envelope membranes that is descended from the cyanobacterial endosymbiont. In plastids of other lineages, the interval between the inner and the outer envelopes at the division site is almost the same as that in other parts of the plastid. In contrast, the inner envelope in glaucophytes constricts faster (accompanied by the ingrowth of the peptidoglycan layer) than the outer envelope membrane, reminiscent of the relationship between the cytoplasmic membrane and the outer membrane in cyanobacterial cell division. Therefore, the interval between the two envelopes at the division site becomes much larger than that in other parts of the chloroplast in glaucophytes (Iino and Hashimoto, 2003; Sato et al., 2009).

Glaucophyte chloroplast division involves FtsZ-based division machinery on the stromal side (Sato et al., 2005, 2009), and a structure similar to the inner PD ring has been detected by electron microscopy. However, the outer PD ring is not evident (Iino and Hashimoto, 2003; Sato et al., 2009). In addition, all of the chloroplast division genes of host origin, including *drp5B*, are absent from the *Cyanophora paradoxa* EST database, where the *ftsZ*, *minD*, and *minE* genes are evident (Miyagishima and Kabeya, 2010). It appears that the outer envelope division in glaucophytes involves a mechanism that is similar to that in bacteria. However, studies on division of the peptidoglycan layer and the outer membrane in bacteria are just beginning (de Boer, 2010). Information from the whole glaucophyte genome, and further studies of bacterial cell wall and outer membrane division, will ultimately clarify the relationship between the loss of the peptidoglycan layer and the evolution of the plastid division machinery.

Peptidoglycans have never been detected in plastids other than glaucophytes, but it should be noted that some algal and plant genomes still encode cyanobacteria-descended proteins that are involved in or related to peptidoglycan synthesis in bacteria. Disruption of the nucleus-encoded *mur* or *mra* genes impairs chloroplast division in the moss *P. patens* (Machida et al., 2006; Homi et al., 2009). The chloroplast genomes of certain green algal lineages still retain *fisI* and *fisW* genes. However, the functions of these gene products in plastids are currently unknown.

Although photosynthesis in eukaryotes largely relies on chloroplasts, numerous eukaryotic species contain bacterial or eukaryotic photosynthetic endo-
CONCLUSION AND PERSPECTIVES

Diverse eukaryotic lineages have acquired photosynthetic activity by endosymbiotic events. Permanent inheritance of photosynthetic endosymbionts or plastids relies on the regulation of endosymbiont or plastid division by the host cell. Recent studies have yielded significant progress in understanding of the mechanism and regulation of plastid division, but many questions still remain to be answered, and new questions are emerging.

The most noteworthy issues concerning the mechanism of plastid division are how the division complex constricts and splits chloroplasts and how the constrictive force is generated. In terms of evolution, another question is whether there are any common trends with regard to the mechanisms that control endosymbiont or organelle division. There likely are, because the evolution of the mitochondrial division machinery is similar to that of plastids. Mitochondria evolved from an α-proteobacterial endosymbiont, and mitochondrial division involves a dynamin-related protein. In addition, mitochondrial division in some eukaryotic lineages also involves the FtsZ protein of α-proteobacterial origin (Kiefel et al., 2006). Further studies should provide important insights not only to the understanding of organelle division but also the mechanisms of membrane fission and eukaryotic evolution effected by endosymbiosis.

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LITERATURE CITED


Miyagishima