Plant Physiology and Biochemistry 135 (2019) 310–321

Contents lists available at ScienceDirect

Plant Physiology and Biochemistry

journal homepage: www.elsevier.com/locate/plaphy

Review

# RNA editing mutants as surrogates for mitochondrial SNP mutants

Mizuki Takenaka[a,*], Anja Jörg[b], Matthias Burger[b], Sascha Haag[b]

[a] Department of Botany, Graduate School of Science, Kyoto University, Oiwake-cho, Sakyo-ku, Kyoto, 606-8502, Japan
[b] Molekulare Botanik, Universität Ulm, Albert-Einstein-Allee 11, 89069, Ulm, Germany

ARTICLE INFO

*Keywords:*
RNA editing
Surrogate mutants
Mitochondria
PPR proteins

ABSTRACT

In terrestrial plants, RNA editing converts specific cytidines to uridines in mitochondrial and plastidic transcripts. Most of these events appear to be important for proper function of organellar encoded genes, since translated proteins from edited mRNAs show higher similarity with evolutionary conserved polypeptide sequences. So far about 100 nuclear encoded proteins have been characterized as RNA editing factors in plant organelles. Respective RNA editing mutants reduce or lose editing activity at different sites and display various macroscopic phenotypes from pale or albino in the case of chloroplasts to growth retardation or even embryonic lethality. Therefore, RNA editing mutants can be a useful resource of surrogate mutants for organellar encoded genes, especially for mitochondrially encoded genes that it is so far unfeasible to manipulate. However, connections between RNA editing defects and observed phenotypes in the mutants are often hard to elucidate, since RNA editing factors often target multiple RNA sites in different genes simultaneously. In this review article, we summarize the physiological aspects of respective RNA editing mutants and discuss them as surrogate mutants for functional analysis of mitochondrially encoded genes.

## 1. Introduction

RNA editing alters the genetic information after transcription. In flowering plants, RNA editing events alter specific cytidines (C) to uridines (U) in plastids and mitochondria (Takenaka et al., 2013a; Hiesel et al., 1989). The number of RNA editing ranges between 30 and 100 and several hundreds in chloroplasts and mitochondria, respectively. However, the number varies in other embryophytes; *Selaginella* and hornworts have a few thousand editing sites in both organelles, while the moss *Physcomitrella* has only 11 in mitochondria and 1 in plastids (Shikanai and Fujii, 2013; Oldenkott et al., 2014; Kugita et al., 2003; Rüdinger et al., 2009; Miyata and Sugita, 2004; Hecht et al., 2011). Despite other liverworts showing RNA editing, no such events were observed in *Marchantiid* liverworts, suggesting that RNA editing was lost in these species (Oda et al., 1992). RNA editing in plant organelles mostly occurs in coding sequences, although also observed in introns, UTR sequences, rRNAs, and tRNAs (Giegé and Brennicke, 1999; Chateigner-Boutin and Small, 2010), RNA editing sometimes generates translational initiation or termination codons and often (approximately 80%) leads to amino acid alterations in the translational products, although there are some exceptions leading to synonymous changes by mostly targeting third codon positions. Proteins translated from edited transcripts increase similarity with evolutionarily conserved sequences, suggesting that most amino acid substitutions by RNA editing in the organellar encoded proteins are likely to be essential for the expression of functional proteins.

More than 100 nuclear encoded proteins required for RNA editing in plant organelles have been characterized in the past 15 years (Sun et al., 2016; Barkan and Small, 2014). Respective RNA editing mutants show variable phenotypes, e.g. severe growth delay (Sung et al., 2010; Zhu et al., 2012; Weiβenberger et al., 2017), yellow leaves (Zhou et al., 2008), albinos (Chateigner-Boutin et al., 2008), reduced enzymatic activity in organelle encoded genes (Okuda et al., 2006, 2009), ABA insensitivity (Murayama et al., 2012), embryonic lethality (Andrés-Colás et al., 2017; Guillaumot et al., 2017; Takenaka et al., 2012) but often no macroscopic phenotypes under laboratory growth conditions (Takenaka, 2010; Zehrmann et al., 2012; Hammani et al., 2009; Takenaka et al., 2010).

Mutants for genes involved in post transcriptional modifications in mitochondrial or plastidic genes have been proposed as “surrogate” mutants due to their potential availability for analyses of organellar encoded proteins (Colas Des Francs-Small and Small, 2014). Among them, mitochondrial RNA editing mutants can be considered as surrogates of single amino acid substituted mutants in mitochondria encoded genes. Thus they are potentially useful tools for analysing detailed functions of mitochondria encoded proteins.

* Corresponding author.
*E-mail address:* mizuki.takenaka@pmg.bot.kyoto-u.ac.jp (M. Takenaka).

https://doi.org/10.1016/j.plaphy.2018.12.014
Received 25 October 2018; Received in revised form 13 December 2018; Accepted 16 December 2018
Available online 17 December 2018

Different RNA editing defects in a mitochondrial gene lead to various phenotypes, due to the distinct impact of respective amino acid substitutions. If multiple editing sites are affected, the mutant plant phenotype can be a result of a synergistic effect. Alternatively, hidden molecular defects other than RNA editing might blind the genuine influence of abolished or reduced RNA editing in the mutants (Weiβenberger et al., 2017; Chateigner-Boutin et al., 2011; Ichinose et al., 2012). Therefore, the causality between the phenotypes of RNA editing mutants and their affected editing events must be carefully discussed.

Here we review so far identified RNA editing factors and phenotypes of their mutants. Furthermore, we discuss biological functions of RNA editing through comparison of RNA editing defects and macroscopic and molecular phenotypes in respective mutants.

## 2. RNA editing factors in plant organelles

### 2.1. Pentatricopeptide repeat (PPR) proteins are specific factors

CRR4, a PPR (pentatricopeptide repeat) protein, was firstly characterized as a factor required for RNA editing in plastids in 2005 (Kotera et al., 2005). Shortly after, another PPR protein, MEF1 (mitochondrial editing factor 1) was identified as the first RNA editing factor in plant mitochondria (Zehrmann et al., 2009). Since then, more than 50 PPR proteins were characterized as specific factors for one or several RNA editing events in plant organelles (Sun et al., 2016). PPR proteins involved in RNA editing belong to the PLS class, in which PPR domains are composed of three PPR variants, P (canonical,35 amino acid), L (long, 35–36 amino acids) and S (short, 31 amino acids) (Lurin and Wide, 2004). PPR domains specifically recognize the sequence 5′ of the respective editing sites. The specificity is likely to be governed by the "PPR code", where amino acid combinations at the 5th and the last positions in respective PPR motifs determine corresponding nucleotide identities (Barkan et al., 2012; Yagi et al., 2013; Takenaka et al., 2013b). According to this rule, the specificity of each PPR motif is not always restricted to a single type of nucleotide but often extents to purine (A/G), or pyrimidine (C/U) nucleotides or shows no significant nucleotide preference. Such "wobble" in the recognition rules partially explains why a single PPR protein is able to target a variety of RNA editing sites, which do not seem to have conserved 5' cis-sequences. Some PPR motif and nucleotide combinations obviously do not follow the PPR code, suggesting that PLS PPR proteins do not require or even avoid tight RNA binding for the RNA editing reaction.

PLS class PPR proteins often harbour a part or an entire C-terminal extension consisting of E1, E2 and DYW domains (Cheng et al., 2016). Both E1 and E2 domains show a PPR motif-like double helix structure, whereas the DYW domain contains the zinc-binding signatures conserved in cytidine deaminases. Thus, it has been proposed that the DYW domain catalyzes the C to U editing reaction. Consistently, if the PPR editing factors lack the DYW domain, other DYW containing proteins with no or only several degenerated PPR motifs (e.g. DYW1, DYW2, MEF8 and MEF8S) are likely to complement it in trans (Andrés-Colás et al., 2017; Guillaumot et al., 2017; Boussardon et al., 2012; Diaz et al., 2017; Verbitskiy et al., 2012a). However, catalytic activity of the DYW domains still needs experimental verification.

### 2.2. Other RNA editing factors

Besides PPR proteins, several nuclear encoded proteins have been characterized as key factors in the RNA editing machinery in plant organelles. MORF/RIP proteins, which compose a small protein family including 9 members, affect several dozen to hundreds of editing sites (Takenaka et al., 2012; Bentolila et al., 2012). These proteins form specific homo- and/or heteromers and interact with PPR type RNA editing factors, suggesting they function in a complex (Zehrmann et al., 2015; Haag et al., 2017). Although the detailed mechanism needs further investigation, structural analyses suggested that the binding of MORF9 to PLS type PPR proteins changes the structure of L motifs and consequently increases their RNA affinity (Yan et al., 2017). RRM (RNA recognition motif) containing proteins are also involved in multiple editing sites in both plant organelles (Tillich et al., 2009; Sun et al., 2013; Shi et al., 2015). These proteins interact with RNAs but less specificity in comparison to PPR proteins. Protein-protein interactions with other RNA editing factors may also be important for their function. PPO1, a key protein for chlorophyll synthesis, is also required for RNA editing in chloroplasts (Zhang et al., 2014). PPO1 interacts with MORF proteins implying that it regulates RNA editing through MORF proteins. A P class PPR protein called NUWA is involved in many RNA editing events in mitochondria despite the fact that other P class PPR proteins act in RNA processing steps other than editing. This protein is proposed to enhance interaction between the short DYW protein, DYW2 and E+ subclass PPR proteins, that have E1, E2 and only a N-terminal part of the DYW domain at the C-terminus (Andrés-Colás et al., 2017; Guillaumot et al., 2017). Another P class PPR protein, PPME (P type PPR Modulating Editing) is essential for RNA editing at two *nad1* sites (Leu et al., 2016). Binding of this PPR protein to the surrounding of the editing sites might affect binding of site-specific PLS type PPR proteins. In contrast to PLS class PPR proteins, which are essential for at most only several sites, other RNA editing factors tend to influence dozens to hundreds of editing sites.

Mutants for these non-PLS PPR type RNA editing factors would not be appropriate as surrogate mutants for mitochondrially encoded genes, since more than 10 target cytidines are affected in various transcripts with various efficiencies. Therefore, we focus on mutants for PLS type PPR proteins in this review. RNA editing sites and their required PPR type factors are listed in Table 1.

## 3. RNA editing mutants as surrogates for SNP mutants

Most mitochondrial proteins are encoded in the nucleus, while several genes are still present in the mitochondrion's own genome. Plant mitochondrial genomes contain up to about 65 functional genes (Richardson et al., 2013; Dong et al., 2018). Although gene contents of mitochondrial genomes are various between species, following several genes encoding membrane proteins of the respiratory chain are retained in mitochondria genomes in land plants: Complex I proteins: *nad1*, *nad2*, *nad3*, *nad4*, *nad4L*, *nad5*, *nad6*, *nad7* and *nad9* genes. Complex III proteins: cob. Complex IV proteins: *cox1*, *cox2*, *cox3*. ATP synthase subunits: *atp1*, *atp4*, *atp6*, *atp8*, *atp9*. Several ccm genes required for cytochrome c maturation: *ccmB*, *ccmC*, *ccmFc*, *ccmFn* and subunits for the ribosome: *rps1*, *rps2*, *rps3*, *rps4*, *rps7*, *rps12*, *rpl2*, *rpl5*, *rpl16* are normally encoded in mitochondria. Additionally, a protein translocator, *mttB* and a maturase required for splicing, *matR* are also present in the mitochondrial genome in many species (Richardson et al., 2013).

The mitochondrial electron transfer chain is composed of four main complexes, comprising subunits of nuclear and mitochondrial origin except for complex II that is fully encoded by the nuclear genome in most land plants. Complex I, the biggest complex, consists of about 40 subunits in plants working as a NADH-ubiquinone oxidoreductase and transfers electrons from NADH to ubiquinone (Braun et al., 2014). Complex III (ubiquinone-cytochrome c oxidoreductase) transfers electrons from ubiquinone to cytochrome c, water-soluble electron carrier. Complex IV (cytochrome c oxidase) further transfers electrons from cytochrome c to molecular oxygen. Protons pumped by these complexes generate a proton motive force that is required for the synthesis of ATP by complex V (ATP synthase). Plant mitochondria have an alternative electron transport pathway, which provides an alternative route for electrons passing through the electron transport chain but will not generate ATP. Since all alternative pathway components are nuclear encoded, they are not affected by RNA editing. The frequency of RNA editing sites is biased among genes, e.g. in Arabidopsis, *atp8* has no editing sites in the transcript, while the similarly sized *nad4* transcript

**Table 1**
Alist of RNA editing mutants with the transcript and position of the editing site affected, amino acid conversion by RNA editing, their species name or AGI number for Arabidopsis, and PPR subclass (Cheng et al., 2016). Additional affected sites in the same mutants, brief description of the phenotypes and data for complex assembly and activity if they are available are also given. Asterisks indicate synonymous substitution by a loss of RNA editing. P: Partially reduced editing sites. n/a: no assays on protein abundance, complex assembly and enzyme activity. (a) If there are two editing sites within a codon, the effect of an editing event to the amino acid sequence depends on the editing status at the other site. In total, 57 editing factors are listed in this table. Several web-based databases for RNA editing sites as well as editing factors are helpful to obtain further information (Lenz et al., 2018; Lo Giudice et al., 2018; Li et al., 2018c).

Complex I

| RNA | sites | AA conversion by editing | Mutated genes | PPR subclass | AGI number | Other affected sites | Phenotypes | Complex accumulation | Ref. |
|---|---|---|---|---|---|---|---|---|---|
| ***nad1*** | 265 | R89W | *GRS1* | E+ | At4g32430 | nad4L-55, nad6-103, rps4-377 | Very slow growth | Very reduced C I | Xie et al. (2016) |
| ***nad1*** | 308 | S103L | *MEF25* | E+ | At3g25060 | | No macroscopic phenotype | n/a | Arenas-M et al. (2013) |
| ***nad1*** | 571 | L191F | *MEF32* | E2 | At4g14170 | cox2-27 *, ccmB-569 | No macroscopic phenotype | n/a | Takenaka et al. (2013b) |
| ***nad1*** | 898 | R300W | *PPME* | P | At3g18020 | nad1-937 | Slow growth | Low NADH dehydrogenase activity | Leu et al. (2016) |
| ***nad1*** | 937 | P313S | *PPME* | P | At3g18020 | nad1-898 | Slow growth | Low NADH dehydrogenase activity | Leu et al. (2016) |
| ***nad2*** | 59 | S30F | *MEF13* | E+ | At3g02330 | nad4-158, nad5-1916, nad7-213 *, cox3-314, ccmFc-50, ccmFc-415, nad5-1665 * | Slow growth | n/a | Glass et al. (2015) |
| ***nad2*** | 558 (P) | S186S* | *REME1* | DYW | At2g03880 | mttB-552 * | No macroscopic phenotype | n/a | Bentolila et al. (2010) |
| ***nad2*** | 842 | S281F | *MEF10* | E2 | At3g11460 | | No macroscopic phenotype | n/a | Härtel et al. (2013a) |
| ***nad2*** | 1160 | S387L | *MEF1* | DYW | At5g52630 | nad7-963, rps4-956 | No macroscopic phenotype | n/a | Zehrmann et al. (2009) |
| ***nad2*** | 1433 | S478L | *MEF7* | DYW | At5g09950 | nad4L-41, cob-325, ccmB-28, | No macroscopic phenotype | n/a | Zehrmann et al. (2012) |
| ***nad2*** | 1457 | S486L | *OGR1* | DYW | Oryza sativa | nad4-401, nad4-416, nad4-433, cox2-167, cox3-572, ccmC-458 | Opaque endosperm | n/a | Kim et al. (2009) |
| ***nad3*** | 61 (P) | P21S or L21L* (a) | *DEK10* | E+ | Zea mays | cox2-550, nad3-62 (P) | Small kernel and delayed development | Reduced C IV, normal C I but low NADH dehydrogenase activity | Qi et al. (2017) |
| ***nad3*** | 62 (P) | P21L or S21L (a) | *DEK10* | E+ | Zea mays | cox2-550, nad3-61 (P) | Small kernel and delayed development | Reduced C IV, normal C I but low NADH dehydrogenase activity | Qi et al. (2017) |
| ***nad3*** | 149 (P) | S50F | *MEF22* | DYW | At3g12770 | | No macroscopic phenotype | n/a | Takenaka et al. (2010) |
| ***nad3*** | 155 | P52L | *PPS1* | DYW | Oryza sativa | nad3-172, nad3-173, nad3-190, nad3-191 | Delayed development and partial pollen sterility | Reduced C I and C I + III | Xiao et al. (2018a) |
| ***nad3*** | 172 | P58S or L58L * (a) | *PPS1* | DYW | Oryza sativa | nad3-155, nad3-173, nad3-190, nad3-191 | Delayed development and partial pollen sterility | Reduced C I and C I + III | Xiao et al. (2018a) |
| ***nad3*** | 173 | P58L or S58L (a) | *PPS1* | DYW | Oryza sativa | nad3-172, nad3-155, nad3-190, nad3-191 | Delayed development and partial pollen sterility | Reduced C I and C I + III | Xiao et al. (2018a) |
| ***nad3*** | 190 | P64S or L64L* (a) | *PPS1* | DYW | Oryza sativa | nad3-172, nad3-173, nad3-155, nad3-191 | Delayed development and partial pollen sterility | Reduced C I and C I + III | Xiao et al. (2018a) |
| ***nad3*** | 191 | P64L or S64L(a) | *PPS1* | DYW | Oryza sativa | nad3-172, nad3-173, nad3-190, nad3-155 | Delayed development and partial pollen sterility | Reduced C I and C I + III | Xiao et al. (2018a) |
| ***nad3*** | 230 | S77L | *PpPPR_56* | DYW | Physcomitrella | nad4-272 | Slow growth | n/a | Ohtani et al. (2010) |
| ***nad3*** | 247 (P) | P83S | *DEK39* | E2 | Zea mays | nad3-247 (partial) | Small kernel and delayed development | Slightly reduced C I and NADH dehydrogenase activity | Li et al. (2018a) |
| ***nad3*** | 250 | P84S | *SLG1* | E+ | At5g08490 | | Slow growth, altered response to abiotic stress | Reduced C I | Yuan and Liu (2012) |
| ***nad3*** | 275 | S92F | *DEK39* | E2 | Zea mays | | Small kernel and delayed development | Slightly reduced C I and NADH dehydrogenase activity | Li et al. (2018a) |
| ***nad4*** | 124 | L42L* | *MEF11* | DYW | At4g14850 | cox3-422, ccmFn2-344, ccmC-568, ccmFn1-378 *, matR-1730 | Slow growth, slightly shorter roots (lovastatin nonsensitive), ABA hypersensitive | No change in C I, CIII, C IV | (Takenaka et al., 2013b; Verbitskiy et al., 2010; Sechet et al., 2015) |
| ***nad4*** | 158 | P53L | *MEF13* | E+ | At3g02330 | nad2-59, nad5-1916, nad7-213*, cox3-314, ccmFc-50, ccmFc-415, nad5-1665 * | Slow growth | n/a | Glass et al. (2015) |
| ***nad4*** | 166 (P) | R56W | *MEF26* | DYW | At3g03580 | cox3-311 | No macroscopic phenotype | n/a | Arenas-M et al. (2014) |
| ***nad4*** | 272 | S91L | *PpPPR_56* | DYW | Physcomitrella | nad3-230 | Slow growth | n/a | Ohtani et al. (2010) |
| ***nad4*** | 376 | R126C | *AHG11* | E+ | At2g44880 | | ABA hypersensitive | n/a | Murayama et al. (2012) |

(*continued on next page*)

**Table 1** (*continued*)

| Complex I | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| RNA | sites | AA conversion by editing | Mutated genes | PPR subclass | AGI number | Other affected sites | Phenotypes | Complex accumulation | Ref. |
| ***nad4*** | 401 | S134L | *OGR1* | DYW | Oryza sativa | nad2-1457, nad4-416, nad4-433, cox2-167, cox3-572, ccmC-458 | Opaque endosperm | n/a | Kim et al. (2009) |
| ***nad4*** | 416 | P139L | *OGR1* | DYW | Oryza sativa | nad4-401, nad2-1457, nad4-433, cox2-167, cox3-572, ccmC-458 | Opaque endosperm | n/a | Kim et al. (2009) |
| ***nad4*** | 433 | L145F | *OGR1* | DYW | Oryza sativa | nad4-401, nad4-416, nad2-1457, cox2-167, cox3-572, ccmC-458 | Opaque endosperm | n/a | Kim et al. (2009) |
| ***nad4*** | 449 | P150L | *SLO1* | E+ | At2g22410 | nad9-328 | Late germination, slow growth | n/a | Sung et al. (2010) |
| ***nad4*** | 1033 | P345S | *SLO4* | E | At4g38010 | | Growth retardation, short roots, late flowering | Reduced C I | Weiβenberger et al. (2017) |
| ***nad4*** | 1129 | L377F | *COD1* | E+ | At2g35030 | cox2-253, cox2-698 | Embryonic lethality | Reduced C IV | Dahan et al. (2014) |
| ***nad4*** | 1355 | S452L | *MEF18* | E | At5g19020 | | No macroscopic phenotype | n/a | Takenaka et al. (2010) |
| ***nad4*** | 1373 | S458F | *MEF35* | DYW | At4g14050 | cob-286, rpl16-209 | No macroscopic phenotype | n/a | Brehme et al. (2015) |
| ***nad4L*** | 41 | S14F | *MEF7* | E+ | At5g09950 | nad2-1433, cob-325, ccmB-28, | No macroscopic phenotype | n/a | Zehrmann et al. (2012) |
| ***nad4L*** | 55 | R19W | *GRS1* | E+ | At4g32430 | nad1-265, nad6-103, rps4-377 | Very slow growth | Very reduced C I | Xie et al. (2016) |
| ***nad4L*** | 110 | S37L | *SLO2* | E+ | At2g13600 | nad7-739, mttB-144 *, mttB-145 | Growth retardation, short roots, late flowering | Reduced C I, C III and C IV | Zhu et al. (2012) |
| ***nad5*** | 374 | P125L | *MEF12* | E+ | At3g09040 | | No macroscopic phenotype | n/a | Härtel et al. (2013b) |
| ***nad5*** | 598 | R200C | *CWM1* | E+ | At1g17630 | ccmB-428, ccmC 463 | Tolerance to a cellulose synthase inhibitor | Decreased cytochrome c,reduced C I, increased C IV | Hu et al. (2016) |
| ***nad5*** | 598 | R200C | *PpPPR_79* | DYW | Physcomitrella | | Slow growth | n/a | Uchida et al. (2011) |
| ***nad5*** | 730 | R244W | *PpPPR_91* | DYW | Physcomitrella | | Very slow growth | n/a | Ohtani et al. (2010) |
| ***nad5*** | 1550 | T517I | *MEF29* | DYW | At4g30700 | cob-908 | No macroscopic phenotype | n/a | Sosso et al. (2012) |
| ***nad5*** | 1550 | T517I | *PPR2263* | DYW | Zea mays | cob-908 | Small kernel and delayed development | Normal C I Activity, reduced C III | Sosso et al. (2012) |
| ***nad5*** | 1580 (P) | S527L | *AEF1/ MPR25* | E+ | At3g22150 | plastids atpF | Pale and slow growth | n/a | Yap et al. (2015) |
| ***nad5*** | 1580 | S527L | *MPR25* | E+ | Oryza sativa | | Slow growth | Normal C I | Toda et al. (2012) |
| ***nad5*** | 1665 | L555L* | *MEF13* | E+ | At3g02330 | nad4-158, nad5-1916, nad7-213 *, cox3-314, ccmFc-50, ccmFc-415, nad2-59 | Slow growth | n/a | Glass et al. (2015) |
| ***nad5*** | 1916 | S639F | *MEF13* | E+ | At3g02330 | nad4-158, nad2-59, nad7-213*, cox3-314, ccmFc-50, ccmFc-415, nad5-1665* | Slow growth | n/a | Glass et al. (2015) |
| ***nad6*** | 103 | R35C | *GRS1* | E+ | At4g32430 | nad4L-55, nad1-265, rps4-377 | Very slow growth | Very reduced C I | Xie et al. (2016) |
| ***nad7*** | 24 | I8I* | *OTP87* | E2 | At1g74600 | atp1-1178 | Late germination, slow growth | Reduced ATPase and F1 complex | Hammani et al. (2011) |
| ***nad7*** | 200 | S67F | *MEF9* | E2 | At1g62260 | | No macroscopic phenotype | n/a | Takenaka (2010) |
| ***nad7*** | 213 | D71D* | *MEF13* | E+ | At3g02330 | nad4-158, nad5-1916, nad2-59, cox3-314, ccmFc-50, ccmFc-415, nad5-1665 * | Slow growth | n/a | Glass et al. (2015) |
| ***nad7*** | 383 (P) | S128L | *DEK36* | E+ | Zea mays | ccmFc-302(P),nad7-383 (p) | Arrested embryogenesis | Reduced C I, C III, C IV | Wang et al. (2017) |
| ***nad7*** | 739 | L247F | *SLO2* | E+ | At2g13600 | nad4L-110, mttB-144 *, mttB-145 | Growth retardation, short roots, late flowering | Reduced C I, C III and C IV | Zhu et al. (2012) |
| ***nad7*** | 836 | P279L | *SMK1* | E+ | Oryza sativa | | Embryo lethality | C I reduction | Li et al. (2014) |
| ***nad7*** | 836 | P279L | *SMK1* | E+ | Zea mays | | Small kernel and arrested embryogenesis | n/a | Li et al. (2014) |
| ***nad7*** | 963 | S321S* | *MEF1* | DYW | At5g52630 | nad2-1160, rps4-956 | No macroscopic phenotype | n/a | Zehrmann et al. (2009) |
| ***nad9*** | 92 | S31F | *MEF57* | DYW | At5g44230 | | No macroscopic phenotype | n/a | Andrés-Colás et al. (2017) |
| ***nad9*** | 328 | R110W | *SLO1* | E+ | At2g22410 | nad4-449 | Late germination, slow growth | n/a | Sung et al. (2010) |
| Complex III | | | | | | | | | |
| RNA | sites | AA conversion by editing | Mutated genes | PPR subclass | AGI number | Other affected sites | Phenotypes | Complex accumulation | Ref. |
| ***cob*** | 286 | L96F | *MEF35* | DYW | At4g14050 | nad4-1373, rpl16-209 | No macroscopic phenotype | n/a | Brehme et al. (2015) |

(*continued on next page*)

**Table 1** (*continued*)

| Complex I | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| RNA | sites | AA conversion by editing | Mutated genes | PPR subclass | AGI number | Other affected sites | Phenotypes | Complex accumulation | Ref. |
| ***cob*** | 325 | H109Y | *MEF7* | DYW | At5g09950 | nad4L-41, nad2-1433, ccmB-28, | No macroscopic phenotype | n/a | Zehrmann et al. (2012) |
| ***cob*** | 908 | P303L | *MEF29* | DYW | At4g30700 | nad5-1550 | No macroscopic phenotype | n/a | Sosso et al. (2012) |
| ***cob*** | 908 | P303L | *PPR2263* | DYW | Zea mays | nad5-1550 | Small kernel and delayed development | Normal C I Activity, reduced C III | Sosso et al. (2012) |
| Complex IV | | | | | | | | | |
| RNA | sites | AA conversion by editing | Mutated genes | PPR subclass | AGI number | Other affected sites | Phenotypes | Complex accumulation | Ref. |
| ***cox1*** | 755 | S252L | *PpPPR_78* | DYW | Physcomitrella | rps14-137 | Slow growth | n/a | (Uchida et al., 2011; Rüdinger et al., 2011) |
| ***cox2*** | 27 | F9F | *MEF32* | E2 | At4g14170 | nad1-571, ccmB-569 | No macroscopic phenotype | n/a | Takenaka et al. (2013b) |
| ***cox2*** | 167 | S56L | *OGR1* | DYW | Oryza sativa | nad4-401, nad4-416, nad4-433, nad2-1457 cox3-572, ccmC-458 | Opaque endosperm | n/a | Kim et al. (2009) |
| ***cox2*** | 253 | R85W | *COD1* | E+ | At2g35030 | cox2-698, nad4-1129 | Embryo lethality | Reduced C IV | Dahan et al. (2014) |
| ***cox2*** | 370 | R124W | *PpPPR_77* | DYW | Physcomitrella | cox3-733 | Very slow growth | n/a | Ohtani et al. (2010) |
| ***cox2*** | 449 | T150M | *EMP18* | DYW | Zea mays | atp6-635 | Arrested embryogenesis | Reduced ATP synthase, no C IV reduction | Li et al. (2018b) |
| ***cox2*** | 550 | P184S | *DEK10* | E+ | Zea mays | nad3-61 (P), nad3-62 (P) | Small kernel and delayed development | Reduced C IV, normal C I but low NADH dehydrogenase activity | Qi et al. (2017) |
| ***cox2*** | 698 | T233M | *COD1* | E+ | At2g35030 | nad4-1129, cox2-253 | embryo lethality | Reduced C IV | Dahan et al. (2014) |
| ***cox3*** | 257 | S86F | *MEF21* | E+ | At2g20540 | | No macroscopic phenotype | n/a | Takenaka et al. (2010) |
| ***cox3*** | 311 | S104F | *MEF26* | DYW | At3g03580 | nad4-166 (P) | No macroscopic phenotype | n/a | Arenas-M et al. (2014) |
| ***cox3*** | 314 | S105F | *MEF13* | E+ | At3g02330 | nad4-158, nad5-1916, nad7-213 *, nad2-59, ccmFc-50, ccmFc-415, nad5-1665 * | Slow growth | n/a | Glass et al. (2015) |
| ***cox3*** | 422 | P141L | *MEF11* | DYW | At4g14850 | nad4-124, ccmFn2-344, ccmC-568, ccmFn1-378, matR-1730 | Slow growth, slightly shorter roots (lovastatin nonsensitive), ABA hypersensitive | No change in C I, C III, C IV | (Takenaka et al., 2013b; Verbitskiy et al., 2010; Sechet et al., 2015) |
| ***cox3*** | 572 | S191F | *OGR1* | DYW | Oryza sativa | nad4-401, nad4-416, nad4-433, cox2-167, nad2-1457, ccmC-458 | Opaque endosperm | n/a | Kim et al. (2009) |
| ***cox3*** | 733 | R245W | *PpPPR_77* | DYW | Physcomitrella | cox2-370 | Very slow growth | n/a | Ohtani et al. (2010) |
| Cytochrome *c* and *c*1 maturation | | | | | | | | | |
| RNA | sites | AA conversion by editing | Mutated genes | PPR subclass | AGI number | Other affected sites | Phenotypes | Complex accumulation | Ref. |
| ***ccmB*** | 28 | H10Y | *MEF7* | DYW | At5g09950 | nad4L-41, cob-325, nad2-1433 | No macroscopic phenotype | n/a | Zehrmann et al. (2012) |
| ***ccmB*** | 43 | P15S | *EMP9* | E+ | Zea mays | rps4-335 | Arrested embryogenesis | Reduced C I, C III, C IV | Yang et al. (2017) |
| ***ccmB*** | 428 (P) | S143L | *CWM1* | E+ | At1g17630 | nad5-598, ccmC-463 | Tolerance to a cellulose synthase inhibitor | Decreased cytochrome c, reduced C I, increased C IV | Martin et al. (2009) |
| ***ccmB*** | 566 | S189F | *MEF19* | E2 | At3g05240 | | No macroscopic phenotype | n/a | Takenaka et al. (2010) |
| ***ccmB*** | 569 | S190F | *MEF32* | E2 | At4g14170 | cox2-27 *, nad1-571 | No macroscopic phenotype | n/a | Takenaka et al. (2013b) |
| ***ccmC*** | 458 | S153L | *OGR1* | DYW | Oryza sativa | nad4-401, nad4-416, nad4-433, cox2-167, con3-572, nad2-1457 | Opaque endosperm | n/a | Kim et al. (2009) |
| ***ccmC*** | 463 | R155C | *CWM1* | E+ | At1g17630 | nad5-598, ccmB-428 (P) | Tolerance to a cellulose synthase inhibitor | Decreased cytochrome c, reduced C I, increased C IV | Martin et al. (2009) |
| ***ccmC*** | 568 | P190S | *MEF11* | DYW | At4g14850 | cox3-422, ccmFn2-344, nad4-124, ccmFn1-378 *, matR-1730 | Slow growth, slightly shorter roots (lovastatin nonsensitive), ABA hypersensitive | No change in C I, C III, C IV | (Takenaka et al., 2013b; Verbitskiy et al., 2010; Sechet et al., 2015) |
| ***ccmC*** | 575 (P) | P192L | *CWM2* | E+ | At1G32415 | | Tolerance to a cellulose synthase inhibitor | Decreased cytochrome c, increased C IV, increased C I + III | |
| ***ccmFc*** | 50 | P17L | *MEF13* | E+ | At3g02330 | nad4-158, nad5-1916, nad7-213*, cox3-314, nad2-59, ccmFc-415, nad5-1665 * | Slow growth | n/a | Glass et al. (2015) |

(*continued on next page*)

**Table 1** (*continued*)

| Complex I | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| RNA | sites | AA conversion by editing | Mutated genes | PPR subclass | AGI number | Other affected sites | Phenotypes | Complex accumulation | Ref. |
| ***ccmFc*** | 103 | P35S | *PpPPR_65* | DYW | Physcomitrella | | Very slow growth | n/a | (Schallenberg-Rüdinger et al., 2013; Ichinose et al., 2013) |
| ***ccmFc*** | 122 | S41F | *PpPPR_71* | DYW | Physcomitrella | | Very slow growth | n/a | Tasaki et al. (2010) |
| ***ccmFc*** | 302 (P) | P101L | *DEK36* | E+ | Zea mays | ccmFc-302(P), nad7-383 (P) | Arrested embryogenesis | Reduced C I, C III, C IV | Wang et al. (2017) |
| ***ccmFc*** | 415 | L139F | *MEF13* | E+ | At3g02330 | nad4-158, nad5-1916, nad7-213 *, cox3-314, ccmFc-50, nad2-59, nad5-1665 * | Slow growth | n/a | Glass et al. (2015) |
| ***ccmFc*** | 543 | V181V* | *PGL1* | DYW | Oryza sativa | plastids ndhD-878 | Pale green | n/a | Xiao et al. (2018b) |
| ***ccmFn1*** | 378 | F126F* | *MEF11* | DYW | At4g14850 | cox3-422, ccmFn2-344, ccmC-568, nad4-124, matR-1730 | Slow growth, slightly shorter roots (lovastatin nonsensitive), ABA hypersensitive | No change in C I, C III, C IV | (Takenaka et al., 2013b; Verbitskiy et al., 2010; Sechet et al., 2015) |
| ***ccmFn1*** | 1553 | S518F | *EMP7* | E2 | Zea mays | | Arrested embryogenesis | Reduced CCM and C III | Sun et al. (2015) |
| ***ccmFn2*** | 176 | P59L | *OTP71* | E2 | At1g64310 | | No macroscopic phenotype | n/a | Chateigner-Boutin et al. (2013) |
| ***ccmFn2*** | 344 | P115L | *MEF11* | DYW | At4g14850 | cox3-422, nad4-124, ccmC-568, ccmFn1-378 *, matR-1730 | Slow growth, slightly shorter roots (lovastatin nonsensitive), ABA hypersensitive | No change in C I, C III, C IV | (Takenaka et al., 2013b; Verbitskiy et al., 2010; Sechet et al., 2015) |
| ATP synthase | | | | | | | | | |
| RNA | sites | AA conversion by editing | Mutated genes | PPR subclass | AGI number | Other affected sites | Phenotypes | Complex accumulation | Ref. |
| ***atp1*** | 1178 | S393L | *OTP87* | E2 | At1g74600 | nad7-24 * | Late germination, slow growth | Reduced ATPase and F1 complex | Hammani et al. (2011) |
| ***atp4*** | 59 | S20F | *DEK36* | E+ | Zea mays | ccmFc-302(P), nad7-383 (P) | Arrested embryogenesis | Reduced C I, C III, C IV | Wang et al. (2017) |
| ***atp4*** | 89 | S30L | *MEF3* | E2 | At1g06140 | | No macroscopic phenotype | n/a | Verbitskiy et al. (2012b) |
| ***atp6*** | 635 | P212L | *EMP18* | DYW | Zea mays | cox2-449 | Arrested embryogenesis | Reduced ATP synthase, normal C IV | Li et al. (2018b) |
| ***atp9*** | 92 | S31L | *PpPPR_98* | DYW | Physcomitrella | | Lethal (no KO lines) | n/a | (Schallenberg-Rüdinger et al., 2013; Ichinose et al., 2013) |
| Translational machinery | | | | | | | | | |
| RNA | sites | AA conversion by editing | Mutated genes | PPR subclass | AGI number | Other affected sites | Phenotypes | Complex accumulation | Ref. |
| ***rpl16*** | 440 | P147L | *OTP72* | E+ | At3g13880 | | No macroscopic phenotype | n/a | Chateigner-Boutin et al. (2013) |
| ***rpl16*** | 458 | P153L | *EMP5* | DYW | Zea mays | | Arrested embryogenesis | n/a | Liu et al. (2013) |
| ***rps14*** | 137 | S46L | *PpPPR_78* | DYW | Physcomitrella | cox1-755 | Slow growth | n/a | (Uchida et al., 2011; Rüdinger et al., 2011) |
| ***rps3*** | 1534 (P) | R512C | *REME2* | DYW | At4g15720 | rps4-175 | No macroscopic phenotype | n/a | Bentolila et al. (2013) |
| ***rps4*** | 175 (P) | P59S | *REME2* | DYW | At4g15720 | rps3-1534 | No macroscopic phenotype | n/a | Bentolila et al. (2013) |
| ***rps4*** | 226 | P76S | *MEF20* | E2 | At3g18970 | | No macroscopic phenotype | n/a | Takenaka et al. (2010) |
| ***rps4*** | 335 | P112L | *EMP9* | E+ | Zea mays | ccmB-43 | Arrested embryogenesis | Reduced C I, C III, C IV | Yang et al. (2017) |
| ***rps4*** | 377 | P126L | *GRS1* | E+ | At4g32430 | nad4L-55, nad6-103, nad1-265 | Very slow growth | Very reduced C I | Xie et al. (2016) |
| ***rps4*** | 956 | S319L | *MEF1* | DYW | At5g52630 | nad7-963 *, nad2-1160 | No macroscopic phenotype | n/a | Zehrmann et al. (2009) |
| Others | | | | | | | | | |
| RNA | sites | AA conversion by editing | Mutated genes | PPR subclass | AGI number | Other affected sites | Phenotypes | Complex accumulation | Ref. |
| ***matR*** | 1895 | S632L | *MEF14* | DYW | At3g26780 | | No macroscopic phenotype | n/a | Verbitskiy et al. (2011) |
| ***mttB*** | 144 | F48F* | *SLO2* | E+ | At2g13600 | nad7-739, nad4L-110, mttB-145 | Growth retardation, short roots, late flowering | Reduced C I, CIII and C IV | Zhu et al. (2012) |
| ***mttB*** | 145 | P49S | *SLO2* | E+ | At2g13600 | nad7-739, mttB-144 *, nad4L-110 | Growth retardation, short roots, late flowering | Reduced C I, CIII and C IV | Zhu et al. (2012) |
| ***mttB*** | 552 (P) | S184S* | *REME1* | DYW | At2g03880 | nad2-558 * | No macroscopic phenotype | n/a | Bentolila et al. (2010) |
| ***mttB*** | 581 | P194L | *MEF31* | E2 | At2g46050 | | No macroscopic phenotype | n/a | Arenas-M et al. (2018) |

contains many of them. Interestingly, the number of editing sites in each gene varies between plant species (Edera et al., 2018).

Most RNA editing events substitute amino acids in the mitochondrially encoded proteins. The RNA editing sites seem to be non-random and significantly biased towards involvement in helices and protein structural cores. RNA editing often converts codons for hydrophilic to hydrophobic amino acids (Yura and Go, 2008; Yura et al., 2009). Therefore, only the edited form of an mRNA can be translated into a polypeptide, which preferably forms helix and core residues at the appropriate positions. These observations suggest that RNA editing events are required for a protein to form a functional three-dimensional structure, which may affect protein-protein interactions within a complex or supercomplex (Yura and Go, 2008; Yura et al., 2009). Hence, RNA editing mutants can be valuable tools to analyse detailed complex assembly in plant mitochondria. In the next sections, We summarize the phenotypes of RNA editing mutants for each mitochondrial complex.

### 3.1. RNA editing mutants for complex I

Transcripts of nine mitochondrially encoded genes for complex I components (*nad1*, *nad2*, *nad3*, *nad4*, *nad4L*, *nad5*, *nad6*, *nad7* and *nad9*) are frequently targeted by C to U RNA editing machinery (Kugita et al., 2003; Giegé and Brennicke, 1999; Edera et al., 2018). The membrane arm of complex I (P module) consists of approximately 27 nuclear encoded proteins and seven mitochondrially encoded subunits (NAD1, NAD2, NAD3, NAD4, NAD4L, NAD5 and NAD6), while the subunits composing the peripheral arm (Q module) are all encoded in the nucleus except for Nad7 and Nad9 (Braun et al., 2014).

So far several mutants for RNA editing in mitochondrially encoded complex I subunits have been described. Some of them show macroscopic and physiological phenotypes, although they are different depending on the particular mutant. The PPR protein SLG1 is required for editing at a site in the *nad3* transcript (*nad3*-250) in *Arabidopsis*. The *slg1*mutant harbours only a NAD3 protein translated from an unedited *nad3* transcript and shows slow growth and altered response to abiotic stresses (Yuan and Liu, 2012). AHG11 is essential for editing at *nad4*-376 and its disrupted mutant exhibits weak hypersensitivity to ABA. The germinating *ahg11* seeds express higher level of ROS-responsive genes (Murayama et al., 2012). The *slo4* mutant abolishes RNA editing at *nad4*-1033, displays a slow growth phenotype and decreased the amount of Complex I and NADH dehydrogenase activity (Weiβenberger et al., 2017). Mutations in the SMK1 gene abolish editing at the 836th nucleotide from the initiation codon in the *nad7* transcript in both maize and rice. The *smk1* mutants exhibit arrested embryo and endosperm development in both plants. Blue-Native gel analyses revealed that the abundance of complex I and supercomplex I + III decreased dramatically in the mutant lines (Li et al., 2014). A mutation in the *AtGRS1*gene leads to a slow growth phenotype and to a lack of RNA editing in *nad1*, *nad4L*, *nad6* and *rps4*. One dimensional Blue-Native gel analysis for mitochondrial complexes clearly demonstrated reduced complex I and almost no NADH dehydrogenase activity, while other complexes appeared to be normal (Xie et al., 2016). DEK39 is required for editing at *nad3*-257 and knock-out lines of this gene show delayed embryos and seedlings. NADH dehydrogenase activity of the complex I is slightly reduced (Li et al., 2018a). The *slo1* mutant completely abolishes editing at sites of the *nad4* and *nad9* transcripts and displays late germination and severe growth retardation (Sung et al., 2010). The protein PPS1 in rice is required for RNA editing at five consecutive sites in *nad3* mRNA. Knock-down or disruption of this gene induces delayed development and partial pollen sterility. The amount of stable NAD3 protein and complex I and III supercomplex in the mutant lines was lower than in the wild type (Xiao et al., 2018a). Physcomitrella RNA editing mutants for *PpPPR_56* display no editing in *nad3* transcripts and slightly reduced growth, whereas mutants for PpPPR_79 and *PpPPR_91* show no editing at *nad5*-598 *and nad5*-730, respectively, and severe growth retardation (Ohtani et al., 2010; Uchida et al., 2011).

Although the amount of complex I and NADH dehydrogenase activity were not always analysed in these mutants, in general, the mutants display more severe growth retardation when they exhibit less amounts of complex I and/or NADH dehydrogenase activity. Accordingly, alternative oxidases are up-regulated in these mutant plants in a similar manner to other complex I mutants (Braun et al., 2014).

The study of the *ndufv4* (NADH:ubiquinone oxidoreductase flavoprotein 4) mutant, which is one of the complex I subunits, in *Arabidopsis* (Meyer et al., 2009), natural mitochondrial mutants with CMS phenotype in *Nicotiana sylvestris* (Pla et al., 1995; Gutierres et al., 1997) or the absence of complex I in mistletoe (Senkler et al., 2018), suggested that the absence of complex I is not lethal in plants (Fromm et al., 2016). Consistently, some of RNA editing mutants are also able to survive with undetectable level of complex I (Zhu et al., 2012). However, disruption of carbonic anhydrase genes, which are proposed to participate in the early assembly process of Complex I or *NDUFV1* (NADH:ubiquinone oxidoreductase flavoprotein 1), a key subunit of Complex I, leads to complete loss of Complex I and to embryo lethality (Fromm et al., 2016; Córdoba et al., 2016; Kühn et al., 2015). In contrast, *smk1* mutants display embryo lethality despite still maintaining detectable level of complex I and Complex I + III (Li et al., 2014). Such contradiction on Complex I requirement for embryogenesis suggests the need for further investigation. It is possible that so far reported *Arabidopsis* complex I mutants with embryo lethal phenotypes may have a defect in other essential functions, or undetectable traces of complex I were present in non-lethal mutants. It is also possible that the requirement of complex I or various supercomplexes could depend on plant species.

In addition to so far mentioned mutants displaying relatively strong phenotypes, additional RNA editing mutants for *nad* transcripts have been described (Table 1) These RNA editing mutants for complex I components would be a great addition to study assembly and functions of such complexes in plants.

### 3.2. Mutants for complex III, complex IV and the c-type cytochrome maturation complex

Complex III, IV and the c-type cytochrome maturation complex are functionally linked by cytochrome c. So far isolated RNA editing mutants in these complexes, therefore, have shown similar phenotypes. Complex III (cytochrome bc1 complex) contains only one mitochondrially encoded subunit, cytochrome b (Cob), requiring editing of several cytidines, whereas the other 9–10 subunits are encoded in nucleus (Schertl and Braun, 2014). The cytochrome c oxidase (complex IV) is a transmembrane protein complex composed of 14 subunits in plants (Millar et al., 2004). The three core subunits (Cox1, Cox2, and Cox3) are mitochondrially encoded. There is no RNA editing site in the cox1 gene in *Arabidopsis*, though this is not common in other plants. For example, *Solanum tuberosum*, potato, has five RNA editing sites in the *cox1* gene including a site required for the creation of an initiation codon (Quiñones et al., 1995). The assembly of cytochrome c oxidase requires the presence of holo-cytochrome, though the detailed process how cytochrome c assembles is still not fully understood in plants (Giegé et al., 2008). The cytochrome c apoprotein is nuclearly encoded and imported into the mitochondrial inter-membrane space where its heme cofactor is covalently attached by the CCM (cytochrome c maturation) complex. This CCM complex consists of four mitochondrially encoded subunits (CcmB, CcmC, CcmFn and CcmFc) or five in *Brassicaceae*, since CcmFn is split into CcmFn1 and CcmFn2 here, and three nuclearly encoded subunits (CCMA, CCME and CCMH). The CCM system in plant mitochondria is of the same type as in bacteria (system I) but different from the system used in chloroplasts (system II) or in animal and yeast mitochondria (system III) (Babbitt et al., 2015).

Since disrupting either complex III, complex IV or cytochrome c leads to arrested embryo development, it is reasonable that only a limited number of RNA editing mutants has been described as defective

in functional complexes III, IV and cytochrome c. Maize *ppr2263* is a putative surrogate complex III mutant with delayed germination and reduced growth phenotypes. This protein is essential for editing of sites in the *cob* and *nad5* transcripts. However, normal complex I activity, complex III deficiency and alternative oxidase induction in *ppr2263* implies that the editing defect in *cob* is the cause of the slow growth phenotype (Sosso et al., 2012). COD1 is essential for two *cox2* editing sites as well as a *nad4* site in Arabidopsis. The *cod1* mutant shows embryo lethality but was able to be rescued with a combination of high- and low-sugar content agar medium, supplemented with cofactors and nutrients (Dahan et al., 2014). No complex IV activity was detected in the mutant whereas NADH dehydrogenase activity appears normal like in the wild type, suggesting that the defect in the two *cox2* editing sites confers the impaired complex IV and the developmental phenotypes (Dahan et al., 2014). Maize *dek10* mutants show small kernel and delayed development. RNA editing in this mutant lines in *cox2* is completely abolished while two sites in *nad3* reduced to about 50%. The assembly of complex IV in the mutant was significantly reduced. Complex I was not reduced but the NADH dehydrogenase activity was greatly reduced. Thus the slow growth phenotype of *dek10* is likely due to synergy of defects in the two complexes (Qi et al., 2017). Similarly, a very slow growth phenotype is observed in knock-out lines of the *Physcomitrella PpPPR_77* gene, which is essential for editing at sites in *cox2* and *cox*3 (Ohtani et al., 2010). The severe development phenotypes observed in these mutants presumably derive from a severe shortage of ATP and consequent reduction of ubiquinone in the mitochondrial membrane, which stimulates ROS (reactive oxygen species) production, despite the alternative oxidase pathway is activated to compensate it. In addition to these mutants, there are several RNA editing mutants in complex III or complex IV displaying no significant growth retardation under normal growth chamber condition: *mef7* (cob), *mef35* (*cob*), *ppppr_78* (*cox1*), *mef21* (*cox3*), and *mef26* (*cox3*) (Zehrmann et al., 2012; Uchida et al., 2011; Brehme et al., 2015; Takenaka et al. Brennicke; Arenas-M et al., 2014; Rüdinger et al., 2011) (Table 1).

Disrupting the CCM complex (e.g. the ccmh mutant (Meyer et al., 2005)) also leads to arrested embryonic development at the torpedo stage due to the lack of cytochrome c. Therefore, it is plausible that the editing defects in ccm transcripts also induce severe developmental defect phenotypes. Loss of *EMP7* also leads to an embryo lethal phenotype with a defect of RNA editing in the *ccmFn* transcript at position 1553 from the initiation codon, which is required for converting the 518th amino acid from Serine to Phenylalanine in wild type maize. C-type cytochromes and complex III are notably reduced in the mutant, suggesting that the RNA editing event is critical for assembly of these complexes (Sun et al., 2015). The *Physcomitrella* PpPPR_71 mutant showed no editing at one of the two editing sites in the *ccmFc* transcript, whereas the PpPPR_65 mutant lost editing at both sites. Both mutants displayed poor growth phenotypes. (Schallenberg-Rüdinger et al., 2013; Tasaki et al., 2010). Mutant plants of two PPR proteins, *cwm1* and *cwm2* display defects in cytochrome c maturation and activation of mitochondrial retrograde signalling. The *cwm1* mutant completely lost editing at *ccmB*-428, *ccmC*-463 and *nad*5-598, while the *cwm2* mutation reduced editing to less than 40% at *ccmC*-575 (Hu et al., 2016). Both mutants contain very low amounts of cytochrome c and display shorter roots. Interestingly, these mitochondrial defects increased the tolerance to cell wall damage induced by cellulose deficiency, suggesting a connection between mitochondrial biogenesis and the cell wall. The editing mutants *otp71* (*ccmFn2*) and *mef19* (*ccmC*) do not display any growth phenotypes (Takenaka et al., 2010; Chateigner-Boutin et al., 2013). It is probable that low levels of properly assembled CCM complex are sufficient for the normal growth under laboratory climate chamber conditions.

### 3.3. RNA editing defect in ATP synthase subunits

Mitochondrial $F_1F_O$ ATP synthase is a rotary motor enzyme complex consisting of 15–18 subunits (Dudkina et al., 2005). Among them, five subunits are encoded in the mitochondrial genome, *atp1* (encoding the alpha subunit of $F_1$), *atp4*, *atp6, atp8*, and *atp9* (encoding subunits of $F_O$). Only few RNA editing mutants for this complex have been described, most probably due to the fact, that the lack of mitochondrial ATP synthesis would be lethal. The lack of editing at the 1178th nucleotide of the *atp1* transcript in *otp87* leads to a change of an amino acid in the alpha subunit (position 393) from serine to leucine and results in a reduced growth phenotype in *Arabidopsis*. The analysis of its mitochondrial membranes indicates a problem in the ATP synthase assembly (Hammani et al., 2011). Maize EMP18 is required for editing in *atp*6 and *cox*2 transcripts and disruption of this gene leads to arrested embryo and endosperm development. Although Blue-Native gel analysis of mitochondrial complexes did not show a clear reduction of complex I, the mature $F_1F_O$ATPase holoenzyme amount was reduced and $F_1$-subcomplex was accumulated. On the other hand, the amounts of COX2 and complex IV in the mutant were at the same level as in the wild type, suggesting that the editing defect in *atp*6-635 and the resulting proline at position 212 in ATP6 is pivotal for the assembly of $F_1F_O$ATP synthase (Li et al., 2018b). In the *dek36* mutant, which also shows arrested embryogenesis, one editing site in the *atp*4 transcript is completely abolished while other affected editing sites (*nad*7-383, *ccmFn*-302) are only partially reduced. Blue-Native PAGE analysis did not show a clear reduction of mitochondrial complexes but a reduction of complex I, complex III and complex IV was demonstrated by western blot analysis. Accumulation of ATP synthase subcomplexes was not investigated in this mutant (Wang et al., 2017). In contrast, *Arabidopsis mef3*, which lost editing at a site in the *atp*4 transcript, does not show any obvious macroscopic phenotypes (Verbitskiy et al., 2012b).

Studies of RNA editing mutants on the ATP synthase should provide valuable information on the assembly of this complex molecular machine and new insights on mitochondrial metabolism in plants.

### 3.4. RNA editing in genes for mitochondrial translation machinery

Mitochondria encode many genes essential for their own protein synthesis machinery (26S, 18S and 5S rRNAs; many tRNAs and ribosomal proteins). Mutations in these genes would affect mitochondrial translation and therefore be very critical or even lethal. Maize EMP5 is required for RNA editing in *rpl*16 mRNA and its disrupted mutants display abortion of embryo and endosperm development at early stages (Liu et al., 2013). Mutant lines of *AtGRS1* show abolished editing of one site in the *rps4* transcript in addition to three editing events in *nad* transcripts in Arabidopsis. The *grs1* mutants have almost no complex I despite other complexes are present at the same level as in wild type plants and consequently display a very slow growth phenotype (Xie et al., 2016). Disruption of *EMP9*, a *GRS1* ortholog in maize, reduced amounts of complex I, complex III and complex V, although RNA editing defects in this mutant are described only in *ccmB* and *rps4* (Yang et al., 2017). However, *ZmGRS1/EMP9* can complement the growth phenotype and RNA editing at the *rps4* site in Arabidopsis *grs1/emp9* mutant, suggesting that the editing defect in *rps*4 may be important for the plants growth phenotypes.

Many additional RNA editing mutants in ribosomal protein encoding genes have been identified: two RNA editing mutants for *rps*4: *mef1* and *mef20* (Takenaka et al., 2010; Zehrmann et al., 2009), and two mutants for *rpl*16: *otp72* and *mef3* (Chateigner-Boutin et al., 2013; Verbitskiy et al., 2012b). But none of them show any macroscopic phenotypes when grown under normal climate chamber conditions. In addition, a *Physcomitrella* mutant lacking PpPPR_78 displays altered RNA editing of *rps14* and *cox1,* though it does not show any macroscopic difference from wild type (Uchida et al., 2011; Rüdinger et al., 2011).

### 3.5. Other mitochondrial protein genes

MatR (maturase-related protein) is encoded within intron4 of *nad1* in angiosperms. Knock-down analysis of the matR gene with designed ribozymes and RIP-Chip analysis suggested that this protein associates with many introns including that encoding *matR* itself (Sultan et al., 2016). So far two RNA editing mutants for this gene have been described, *mef11* and *mef14*, neither of them display macroscopic phenotypes (Takenaka et al., 2013b; Verbitskiy et al., 2010, 2011).

The plant mitochondrial genome encodes a *mttB* gene. In bacteria, MTTB is an essential integral membrane protein, which is involved in membrane targeting and secretion of cofactor-containing proteins (Weiner et al., 1998). In angiosperms, MTTB exhibits high similarity to its ortholog in bacteria, and may have a similar function in the mitochondrial membrane of plants (Unseld et al., 1997). However, the function of this gene in plant mitochondria has not yet been identified mainly due to the lack of appropriate mutants for analysis. So far only two RNA editing mutants for *mttB* transcripts have been described. Mutants of *SLO2* show RNA editing defects at the two consecutive sites 144 and 145 in the *mttB* transcript, which convert an amino acid at position 49 from serine to proline, in addition to some sites in *nad* transcripts. Not only complex I but also complex III and IV in the mutant lines are reduced in the mutant lines, implying the defect of RNA editing in *mttB* may inhibit the mitochondrial import of essential proteins for assembly of mitochondrial trans-membrane complexes and consequently reduce the function of those complexes (Zhu et al., 2012). The second mutant is *mef31*, which abolishes the editing site *mttB*-581, but no visible macroscopic phenotype is observed (Arenas-M et al., 2018).

Mutants for splicing have been used as surrogate knock-out lines if target genes have introns as observed in many *nad* genes (Colas Des Francs-Small and Small, 2014). However, absence of introns in these two genes indicates RNA editing mutants are the only possible surrogate mutants. Thus, screening for RNA editing mutants for these genes would be very useful to obtain a clue for their functional analysis.

## 4. Advantage and disadvantage of RNA editing mutants as a source for surrogate mutants for mitochondrial genes

There are various advantages offered by RNA editing mutants. At first, they offer independent single amino acid substituted mutants affected in specific complexes at specific subunits and positions. Since RNA editing events are generally well conserved, it is assumed that the respective single amino acid substitution are most likely physiologically important. The high conservation of editing sites allows comparing the impact of an editing defect on mitochondrial proteins, protein complexes, or plant phenotypes between different land plant species. Secondly, they often provide milder, partial or conditional phenotypes compared to knockout mutants of nuclear encoded proteins (Sung et al., 2010; Zhu et al., 2012; Uchida et al., 2011; Hammani et al., 2011; Sechet et al., 2015; Schallenberg-Rüdinger et al., 2017). These moderate phenotypes can be very useful for analysing essential functions such as mitochondrial translation, ATP synthesis, splicing maturation or *mttB*. Thirdly, the RNA editing mutants, which lost only a part of the function of a single organelle-encoded subunit of a large complex allow us to study the order and detailed conformation of assembly of the different modules of the respective complexes. Consequently, it may also allow us to analyse how the absence of an assembled complex represses the synthesis of some or all of its subunits. This implies a feedback loop from mitochondrial protein complex assembly to translation, whereby unassembled subunits may block translation of their own mRNA.

One of the disadvantages of RNA editing mutants as a surrogate mutant resource for mitochondrial genes is the multiple targetability observed for some editing factors. Since many PPR type RNA editing factors edit not only one cytidine but also several different ones located in different genes, it is hard to distinguish the effect of one editing defect to the others (Zhu et al., 2012; Zehrmann et al., 2009; Verbitskiy et al., 2010; Glass et al., 2015; Kim et al., 2009). To overcome this issue, modification of PPR repeats in RNA editing factors following the “PPR code” to increase target specificity would be very helpful (Barkan et al., 2012; Yagi et al., 2013; Takenaka et al., 2013b). If a PPR protein targeting multiple sites lost its ability to edit one of them, mutant lines complemented with their respective modified PPR protein would be useful to evaluate the effect of the respective uncomplemented RNA editing site. However, so far no such attempts have been successful (Kindgren et al., 2015). Cross competitions with orthologs from different plants may also allow specifying target editing sites, because the targets of orthologs can vary even in closely related species (Edera et al., 2018).

Embryo lethality observed in some RNA editing mutants is another issue for utilizing them as surrogate mutants. RNAi or knock-down lines for RNA editing factors might overcome this problem (Xiao et al., 2018a; Ichinose et al., 2013), although the effect of the remained proper functional proteins translated from edited mitochondrial transcripts should be carefully considered.

## 5. Conclusions

As we reviewed here, many RNA editing mutants with variable phenotypes have been characterized and have contributed to understand mitochondrial biogenesis and functions, suggesting a high potential of these mutants as a tool for further detailed analysis of mitochondria. More comprehensive analysis of them would greatly increase their value. For example, so far even Blue-Native gel analysis, which is a standard method to evaluate mitochondrial complexes, has not always been applied. It would be essential to analyse all editing mutants with a standard set of experiments for comparison of them in detail. Furthermore, reanalysis of many RNA editing mutants that have been described as “no phenotype” may provide valuable outcomes (Table 1). Although normal climate chamber condition did not lead to any phenotypes, such mutants may show some interesting phenotypes under different conditions or with a different view based on features observed in other RNA editing mutants (e.g. hormone response, cell wall synthesis etc.).

## CRediT authorship contribution statement

**Mizuki Takenaka:** Writing – original draft. **Anja Jörg:** Writing – original draft. **Matthias Burger:** Writing – original draft. **Sascha Haag:** Writing – original draft.

## Acknowledgments

This work was supported by Japan Society for the promotion of Science (JSPS) Grants-in-Aid for Scientific Research 18H02462 and Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) grant TA624/10-1 to M.T.

## References

Andrés-Colás, N., Zhu, Q., Takenaka, M., De Rybel, B., Weijers, D., Van Der Straeten, D., 2017. Multiple PPR protein interactions are involved in the RNA editing system in *Arabidopsis* mitochondria and plastids. Proc. Natl. Acad. Sci. Unit. States Am. 114, 201705815. https://doi.org/10.1073/pnas.1705815114.

Arenas-M, A., Takenaka, M., Moreno, S., Gómez, I., Jordana, X., 2013. Contiguous RNA editing sites in the mitochondrial *nad1* transcript of *Arabidopsis thaliana* are recognized by different proteins. FEBS Lett. 587, 887–891. https://doi.org/10.1016/j.febslet.2013.02.009.

Arenas-M, A., Zehrmann, A., Moreno, S., Takenaka, M., Jordana, X., 2014. The pentatricopeptide repeat protein MEF26 participates in RNA editing in mitochondrial cox3 and nad4 transcripts. Mitochondrion 19. https://doi.org/10.1016/j.mito.2014.08.006.

Arenas-M, A., González-Durán, E., Gómez, I., Burger, M., Brennicke, A., Takenaka, M., Jordana, X., 2018. The pentatricopeptide repeat protein MEF31 is required for

editing at site 581 of the mitochondrial tatC transcript and indirectly influences editing at site 586 of the same transcript. Plant Cell Physiol. 59. https://doi.org/10.1093/pcp/pcx190.
Babbitt, S.E., Sutherland, M.C., San Francisco, B., Mendez, D.L., Kranz, R.G., 2015. Mitochondrial cytochrome c biogenesis: no longer an enigma. Trends Biochem. Sci. 40, 446–455. https://doi.org/10.1016/j.tibs.2015.05.006.
Barkan, A., Small, I., 2014. Pentatricopeptide repeat proteins in plants. Annu. Rev. Plant Biol. 65, 415–442. https://doi.org/10.1146/annurev-arplant-050213-040159.
Barkan, A., Rojas, M., Fujii, S., Yap, A., Chong, Y.S., Bond, C.S., Small, I., 2012. A combinatorial amino acid code for RNA recognition by pentatricopeptide repeat proteins. PLoS Genet. 8, e1002910. https://doi.org/10.1371/journal.pgen.1002910.
Bentolila, S., Knight, W., Hanson, M., 2010. Natural variation in Arabidopsis leads to the identification of REME1, a pentatricopeptide repeat-DYW protein controlling the editing of mitochondrial transcripts. Plant Physiol. 154https://doi.org/10.1104/pp.110.165969. 1966–82.
Bentolila, S., Heller, W.P., Sun, T., Babina, a. M., Friso, G., van Wijk, K.J., Hanson, M.R., 2012. PNAS Plus: RIP1, a member of an Arabidopsis protein family, interacts with the protein RARE1 and broadly affects RNA editing. Proc. Natl. Acad. Sci. Unit. States Am. 109, E1453–E1461. https://doi.org/10.1073/pnas.1121465109.
Bentolila, S., Babina, A.M., Germain, A., Hanson, M.R., 2013. Quantitative trait locus mapping identifies REME2, a PPR-DYW protein required for editing of specific C targets in Arabidopsis mitochondria. RNA Biol. 10, 1520–1525. https://doi.org/10.4161/rna.25297.
Boussardon, C., Salone, V., Avon, A., Berthomé, R., Hammani, K., Okuda, K., Shikanai, T., Small, I., Lurin, C., 2012. Two interacting proteins are necessary for the editing of the NdhD-1 site in Arabidopsis plastids. Plant Cell 24, 3684–3694. https://doi.org/10.1105/tpc.112.099507.
Braun, H.-P., Binder, S., Brennicke, A., Eubel, H., Fernie, A.R., Finkemeier, I., Klodmann, J., König, A.-C., Kühn, K., Meyer, E., Obata, T., Schwarzländer, M., Takenaka, M., Zehrmann, A., 2014. The life of plant mitochondrial complex I. Mitochondrion 19. https://doi.org/10.1016/j.mito.2014.02.006.
Brehme, N., Bayer-Császár, E., Glass, F., Takenaka, M., 2015. The DYW subgroup PPR protein MEF35 targets RNA editing sites in the mitochondrial rpl16, nad4 and cob mRNAs in Arabidopsis thaliana. PLoS One 10. https://doi.org/10.1371/journal.pone.0140680.
Chateigner-Boutin, A.-L., Small, I., 2010. Plant RNA editing. RNA Biol. 7, 213–219. https://doi.org/10.4161/rna.7.2.11343.
Chateigner-Boutin, A.L., Ramos-Vega, M., Guevara-García, A., Andrés, C., Gutiérrez-Nava, M.D.L.L., Cantero, A., Delannoy, E., Jiménez, L.F., Lurin, C., Small, I., Leo, P., 2008. CLB19, a pentatricopeptide repeat protein required for editing of rpoA and clpP chloroplast transcripts. Plant J. 56, 590–602. https://doi.org/10.1111/j.1365-313X.2008.03634.x.
Chateigner-Boutin, A.-L., des Francs-Small, C.C., Delannoy, E., Kahlau, S., Tanz, S.K., de Longevialle, A.F., Fujii, S., Small, I., 2011. OTP70 is a pentatricopeptide repeat protein of the E subgroup involved in splicing of the plastid transcript rpoC1. Plant J. 65, 532–542. https://doi.org/10.1111/j.1365-313X.2010.04441.x.
Chateigner-Boutin, A.L., Colas Des Francs-Small, C., Fujii, S., Okuda, K., Tanz, S.K., Small, I., 2013. The e domains of pentatricopeptide repeat proteins from different organelles are not functionally equivalent for RNA editing. Plant J. 74, 935–945.
Cheng, S., Gutmann, B., Zhong, X., Ye, Y., Fisher, M.F., Bai, F., Castleden, I., Song, Y., Song, B., Huang, J., Liu, X., Xu, X., Lim, B.L., Bond, C.S., Yiu, S.-M., Small, I., 2016. Redefining the structural motifs that determine RNA binding and RNA editing by pentatricopeptide repeat proteins in land plants. Plant J. 85, 532–547. https://doi.org/10.1111/tpj.13121.
Colas Des Francs-Small, C., Small, I., 2014. Surrogate mutants for studying mitochondrially encoded functions. Biochimie 100, 234–242. https://doi.org/10.1016/j.biochi.2013.08.019.
Córdoba, J.P., Marchetti, F., Soto, D., Martin, M.V., Pagnussat, G.C., Zabaleta, E., 2016. The CA domain of the respiratory complex I is required for normal embryogenesis in *Arabidopsis thaliana*. J. Exp. Bot. 67, 1589–1603. https://doi.org/10.1093/jxb/erv556.
Dahan, J., Tcherkez, G., Macherel, D., Benamar, a., Belcram, K., Quadrado, M., Arnal, N., Mireau, H., 2014. Disruption of the CYTOCHROME C OXIDASE DEFICIENT1 Gene Leads to Cytochrome C Oxidase Depletion and Reorchestrated Respiratory Metabolism in Arabidopsis. https://doi.org/10.1104/pp.114.248526.
Diaz, M.F., Bentolila, S., Hayes, M.L., Hanson, M.R., Mulligan, R.M., 2017. A protein with an unusually short PPR domain, MEF8, affects editing at over 60 Arabidopsis mitochondrial C targets of RNA editing. Plant J. 92, 638–649. https://doi.org/10.1111/tpj.13709.
Dong, S., Zhao, C., Chen, F., Liu, Y., Zhang, S., Wu, H., Zhang, L., Liu, Y., 2018. The complete mitochondrial genome of the early flowering plant Nymphaea colorata is highly repetitive with low recombination. BMC Genomics 19, 614. https://doi.org/10.1186/s12864-018-4991-4.
Dudkina, N.V., Heinemeyer, J., Keegstra, W., Boekema, E.J., Braun, H.-P., 2005. Structure of dimeric ATP synthase from mitochondria: an angular association of monomers induces the strong curvature of the inner membrane. FEBS Lett. 579, 5769–5772. https://doi.org/10.1016/J.FEBSLET.2005.09.065.
Edera, A.A., Gandini, C.L., Sanchez-Puerta, M.V., 2018. Towards a comprehensive picture of C-to-U RNA editing sites in angiosperm mitochondria. Plant Mol. Biol. 97, 215–231. https://doi.org/10.1007/s11103-018-0734-9.
Fromm, S., Senkler, J., Eubel, H., Peterhänsel, C., Braun, H.-P., 2016. Life without complex I: proteome analyses of an Arabidopsis mutant lacking the mitochondrial NADH dehydrogenase complex. J. Exp. Bot. 67, 3079–3093. https://doi.org/10.1093/jxb/erw165.
Giegé, P., Brennicke, A., 1999. RNA editing in Arabidopsis mitochondria effects 441 C to U changes in ORFs. Proc. Natl. Acad. Sci. U. S. A 96, 15324–15329. https://doi.org/10.1073/PNAS.96.26.15324.
Giegé, P., Grienenberger, J.M., Bonnard, G., 2008. Cytochrome c biogenesis in mitochondria. Mitochondrion 8, 61–73. https://doi.org/10.1016/j.mito.2007.10.001.
Glass, F., Hä Rtel, B., Zehrmann, A., Verbitskiy, D., Takenaka, M., 2015. MEF13 requires MORF3 and MORF8 for RNA editing at eight targets in mitochondrial mRNAs in Arabidopsis thaliana. Mol. Plant 8, 1466–1477. https://doi.org/10.1016/j.molp.2015.05.008.
Guillaumot, D., Lopez-Obando, M., Baudry, K., Avon, A., Rigaill, G., Falcon De Longevialle, A., Broche, B., Takenaka, M., Berthomé, R., De Jaeger, G., Delannoy, E., Lurin, C., 2017. Two interacting PPR proteins are major Arabidopsis editing factors in plastid and mitochondria. Proc. Natl. Acad. Sci. U. S. A 114. https://doi.org/10.1073/pnas.1705780114.
Gutierres, S., Sabar, M., Lelandais, C., Chetrit, P., Diolez, P., Degand, H., Boutry, M., Vedel, F., de Kouchkovsky, Y., De Paepe, R., 1997. Lack of mitochondrial and nuclear-encoded subunits of complex I and alteration of the respiratory chain in Nicotiana sylvestris mitochondrial deletion mutants. Proc. Natl. Acad. Sci. U. S. A 94, 3436–3441. https://doi.org/10.1073/PNAS.94.7.3436.
Haag, S., Schindler, M., Berndt, L., Brennicke, A., Takenaka, M., Weber, G., 2017. Crystal structures of the Arabidopsis thaliana organellar RNA editing factors MORF1 and MORF9. Nucleic Acids Res. https://doi.org/10.1093/nar/gkx099.
Hammani, K., Okuda, K., Tanz, S.K., Chateigner-Boutin, A.-L., Shikanai, T., Small, I., 2009. A study of new Arabidopsis chloroplast RNA editing mutants reveals general features of editing factors and their target sites. Plant Cell 21, 3686–3699. https://doi.org/10.1105/tpc.109.071472.
Hammani, K., Des Francs-Small, C.C., Takenaka, M., Tanz, S.K., Okuda, K., Shikanai, T., Brennicke, A., Small, I., 2011. The pentatricopeptide repeat protein OTP87 is essential for RNA editing of nad7 and atp1 transcripts in Arabidopsis mitochondria. J. Biol. Chem. 286, 21361–21371. https://doi.org/10.1074/jbc.M111.230516.
Härtel, B., Zehrmann, A., Verbitskiy, D., van der Merwe, J.A., Brennicke, A., Takenaka, M., 2013a. MEF10 is required for RNA editing at nad2-842 in mitochondria of Arabidopsis thaliana and interacts with MORF8. Plant Mol. Biol. 81. https://doi.org/10.1007/s11103-012-0003-2.
Härtel, B., Zehrmann, A., Verbitskiy, D., Takenaka, M., 2013b. The longest mitochondrial RNA editing PPR protein MEF12 in Arabidopsis thaliana requires the full-length E domain. RNA Biol. 10, 1543–1548. https://doi.org/10.4161/rna.25484.
Hecht, J., Grewe, F., Knoop, V., 2011. Extreme RNA editing in coding islands and abundant microsatellites in repeat sequences of Selaginella moellendorffii mitochondria: the root of frequent plant mtDNA recombination in early tracheophytes. Genome Biol. Evol. 3, 344–358. https://doi.org/10.1093/gbe/evr027.
Hiesel, R., Wissinger, B., Schuster, W., Brennicke, A., 1989. RNA editing in plant mitochondria. Science 246, 1632–1634. https://doi.org/10.1126/SCIENCE.2480644.
Hu, Z., Vanderhaeghen, R., Cools, T., Wang, Y., De Clercq, I., Leroux, O., Nguyen, L., Belt, K., Millar, A.H., Audenaert, D., Hilson, P., Small, I., Mouille, G., Vernhettes, S., Van Breusegem, F., Whelan, J., Höfte, H., De Veylder, L., 2016. Mitochondrial defects confer tolerance against cellulose deficiency. Plant Cell 28, 2276–2290. https://doi.org/10.1105/tpc.16.00540.
Ichinose, M., Tasaki, E., Sugita, C., Sugita, M., 2012. A PPR-DYW protein is required for splicing of a group II intron of *cox1* pre-mRNA in *Physcomitrella patens*. Plant J. Cell Mol. Biol. 70, 271–278. https://doi.org/10.1111/j.1365-313X.2011.04869.x.
Ichinose, M., Sugita, C., Yagi, Y., Nakamura, T., Sugita, M., 2013. Two DYW subclass PPR proteins are involved in RNA editing of ccmFc and atp9 transcripts in the moss Physcomitrella patens: first complete set of PPR editing factors in plant mitochondria. Plant Cell Physiol. 54, 1907–1916. https://doi.org/10.1093/pcp/pct132.
Kim, S.-R., Yang, J.-I., Moon, S., Ryu, C.-H., An, K., Kim, K.-M., Yim, J., An, G., 2009. Rice OGR1 encodes a pentatricopeptide repeat-DYW protein and is essential for RNA editing in mitochondria. Plant J. 59, 738–749. https://doi.org/10.1111/j.1365-313X.2009.03909.x.
Kindgren, P., Yap, A., Bond, C.S., Small, I., 2015. Predictable alteration of sequence recognition by RNA editing factors from Arabidopsis. Plant Cell 27, 403–416. https://doi.org/10.1105/tpc.114.134189.
Kotera, E., Tasaka, M., Shikanai, T., 2005. A pentatricopeptide repeat protein is essential for RNA editing in chloroplasts. Nature 433, 326–330. https://doi.org/10.1038/nature03229.
Kugita, M., Yamamoto, Y., Fujikawa, T., Matsumoto, T., Yoshinaga, K., 2003. RNA editing in hornwort chloroplasts makes more than half the genes functional. Nucleic Acids Res. 31, 2417–2423.
Kühn, K., Obata, T., Feher, K., Bock, R., Fernie, A.R., Meyer, E.H., 2015. Complete mitochondrial complex I deficiency induces an up-regulation of respiratory fluxes that is abolished by traces of functional complex I. Plant Physiol. 168, 1537–1549. https://doi.org/10.1104/pp.15.00589.
Lenz, H., Hein, A., Knoop, V., 2018. Plant organelle RNA editing and its specificity factors: Enhancements of analyses and new database features in PREPACT 3.0. BMC Bioinfor. 19. https://doi.org/10.1186/s12859-018-2244-9.
Leu, K.-C., Hsieh, M.-H., Wang, H.-J., Hsieh, H.-L., Jauh, G.-Y., 2016. Distinct role of Arabidopsis mitochondrial P-type pentatricopeptide repeat protein-modulating editing protein, PPME, in nad1 RNA editing. RNA Biol. https://doi.org/10.1080/15476286.2016.1184384.
Li, X.J., Zhang, Y.F., Hou, M., Sun, F., Shen, Y., Xiu, Z.H., Wang, X., Chen, Z.L., Sun, S.S.M., Small, I., Tan, B.C., 2014. Small kernel 1 encodes a pentatricopeptide repeat protein required for mitochondrial nad7 transcript editing and seed development in maize (Zea mays) and rice (Oryza sativa). Plant J. 79, 797–809. https://doi.org/10.1111/tpj.12584.
Li, X., Gu, W., Sun, S., Chen, Z., Chen, J., Song, W., Zhao, H., Lai, J., 2018a. Defective Kernel 39 encodes a PPR protein required for seed development in maize. J. Integr. Plant Biol. 60, 45–64. https://doi.org/10.1111/jipb.12602.
Li, X.-L., Huang, W.-L., Yang, H.-H., Jiang, R.-C., Sun, F., Wang, H.-C., Zhao, J., Xu, C.-H.,

Tan, B.-C., 2018b. EMP18 Functions in Mitochondrial *Atp6* and *Cox2* Transcript Editing and Is Essential to Seed Development in Maize, New Phytol. https://doi.org/10.1111/nph.15425.
Li, M., Xia, L., Zhang, Y., Niu, G., Li, M., Wang, P., Zhang, Z., 2018c. Plant editosome database: a curated database of RNA editosome in plants. Nucleic Acids Res. https://doi.org/10.1093/nar/gky1026.
Liu, Y.-J., Xiu, Z.-H., Meeley, R., Tan, B.-C., 2013. Empty pericarp5 encodes a pentatricopeptide repeat protein that is required for mitochondrial RNA editing and seed development in maize. Plant Cell 25, 868–883. https://doi.org/10.1105/tpc.112.106781.
Lo Giudice, C., Pesole, G., Picardi, E., 2018. REDIdb 3.0: a comprehensive collection of rna editing events in plant organellar genomes. Front. Plant Sci. 9, 482. https://doi.org/10.3389/fpls.2018.00482.
Lurin, C., Wide, Genome, 2004. Analysis of Arabidopsis pentatricopeptide repeat proteins reveals their essential role in organelle biogenesis. Plant Cell 16, 2089–2103. https://doi.org/10.1105/tpc.104.022236.
Martin, A., Troadec, C., Boualem, A., Rajab, M., Fernandez, R., Morin, H., Pitrat, M., Dogimont, C., Bendahmane, A., 2009. A transposon-induced epigenetic change leads to sex determination in melon. Nature 461, 1135–1138. https://doi.org/10.1038/nature08498.
Meyer, E.H., Giegé, P., Gelhaye, E., Rayapuram, N., Ahuja, U., Thöny-Meyer, L., Grienenberger, J.-M., Bonnard, G., 2005. AtCCMH, an essential component of the c-type cytochrome maturation pathway in Arabidopsis mitochondria, interacts with apocytochrome c. Proc. Natl. Acad. Sci. U. S. A 102, 16113–16118. https://doi.org/10.1073/pnas.0503473102.
Meyer, E.H., Tomaz, T., Carroll, A.J., Estavillo, G., Delannoy, E., Tanz, S.K., Small, I.D., Pogson, B.J., Millar, A.H., 2009. Remodeled respiration in ndufs4 with low phosphorylation efficiency suppresses Arabidopsis germination and growth and alters control of metabolism at night. Plant Physiol. 151, 603–619. https://doi.org/10.1104/pp.109.141770.
Millar, A.H., Eubel, H., Jänsch, L., Kruft, V., Heazlewood, J.L., Braun, H.P., 2004. Mitochondrial cytochrome c oxidase and succinate dehydrogenase complexes contain plant specific subunits. Plant Mol. Biol. 56, 77–90. https://doi.org/10.1007/s11103-004-2316-2.
Miyata, Y., Sugita, M., 2004. Tissue- and stage-specific RNA editing of rps14 transcripts in moss (Physcomitrella patens) chloroplasts. J. Plant Physiol. 161, 113–115. https://doi.org/10.1078/0176-1617-01220.
Murayama, M., Hayashi, S., Nishimura, N., Ishide, M., Kobayashi, K., Yagi, Y., Asami, T., Nakamura, T., Shinozaki, K., Hirayama, T., 2012. Isolation of Arabidopsis ahg11, a weak ABA hypersensitive mutant defective in nad4 RNA editing. J. Exp. Bot. 63, 5301–5310. https://doi.org/10.1093/jxb/ers188.
Oda, K., Yamato, K., Ohta, E., Nakamura, Y., Takemura, M., Nozato, N., Akashi, K., Kanegae, T., Ogura, Y., Kohchi, T., Ohyama, K., 1992. Gene organization deduced from the complete sequence of liverwort Marchantia polymorpha mitochondrial DNA. A primitive form of plant mitochondrial genome. J. Mol. Biol. 223, 1–7. https://doi.org/10.1016/0022-2836(92)90708-R.
Ohtani, S., Ichinose, M., Tasaki, E., Aoki, Y., Komura, Y., Sugita, M., 2010. Targeted gene disruption identifies three PPR-DYW proteins involved in RNA editing for five editing sites of the moss mitochondrial transcripts. Plant Cell Physiol. 51, 1942–1949. https://doi.org/10.1093/pcp/pcq142.
Okuda, K., Nakamura, T., Sugita, M., Shimizu, T., Shikanai, T., 2006. A pentatricopeptide repeat protein is a site recognition factor in chloroplast RNA editing. J. Biol. Chem. 281, 37661–37667. https://doi.org/10.1074/jbc.M608184200.
Okuda, K., Chateigner-Boutin, A.-L., Nakamura, T., Delannoy, E., Sugita, M., Myouga, F., Motohashi, R., Shinozaki, K., Small, I., Shikanai, T., 2009. Pentatricopeptide repeat proteins with the DYW motif have distinct molecular functions in RNA editing and RNA cleavage in Arabidopsis chloroplasts. Plant Cell 21, 146–156. https://doi.org/10.1105/tpc.108.064667.
Oldenkott, B., Yamaguchi, K., Tsuji-Tsukinoki, S., Knie, N., Knoop, V., 2014. Chloroplast RNA editing going extreme: more than 3400 events of C-to-U editing in the chloroplast transcriptome of the lycophyte Selaginella uncinata. RNA 20, 1499–1506.
Pla, M., Mathieu, C., De Paepe, R., Chétrit, P., Vedel, F., 1995. Deletion of the last two exons of the mitochondrial nad7 gene results in lack of the NAD7 polypeptide in a Nicotiana sylvestris CMS mutant. Mol. Gen. Genet. 248, 79–88. https://doi.org/10.1007/BF02456616.
Qi, W., Tian, Z., Lu, L., Chen, X., Chen, X., Zhang, W., Song, R., 2017. Editing of mitochondrial transcripts nad3 and cox2 by dek10 is essential for mitochondrial function and maize plant development. Genetics 205, 1489–1501. https://doi.org/10.1534/genetics.116.199331.
Quiñones, V., Zanlungo, S., Holuigue, L., Litvak, S., Jordana, X., 1995. The cox1 initiation codon is created by RNA editing in potato mitochondria. Plant Physiol. 108, 1327–1328. https://doi.org/10.1104/pp.108.3.1327.
Richardson, A.O., Rice, D.W., Young, G.J., Alverson, A.J., Palmer, J.D., 2013. The "fossilized" mitochondrial genome of Liriodendron tulipifera: ancestral gene content and order, ancestral editing sites, and extraordinarily low mutation rate. BMC Biol. 11, 29. https://doi.org/10.1186/1741-7007-11-29.
Rüdinger, M., Funk, H.T., Rensing, S.A., Maier, U.G., Knoop, V., 2009. RNA editing: only eleven sites are present in the Physcomitrella patens mitochondrial transcriptome and a universal nomenclature proposal. Mol. Genet. Genom. 281, 473–481. https://doi.org/10.1007/s00438-009-0424-z.
Rüdinger, M., Szövényi, P., Rensing, S. a., Knoop, V., 2011. Assigning DYW-type PPR proteins to RNA editing sites in the funariid mosses Physcomitrella patens and Funaria hygrometrica. Plant J. 67, 370–380. https://doi.org/10.1111/j.1365-313X.2011.04600.x.
Schallenberg-Rüdinger, M., Kindgren, P., Zehrmann, A., Small, I., Knoop, V., 2013. A DYW-protein knockout in Physcomitrella affects two closely spaced mitochondrial editing sites and causes a severe developmental phenotype. Plant J. 76, 420–432. https://doi.org/10.1111/tpj.12304.
Schallenberg-Rüdinger, M., Oldenkott, B., Hiss, M., Le Trinh, P., Knoop, V., Rensing, S.A., 2017. A Single-target mitochondrial RNA editing factor of funaria hygrometrica can fully reconstitute RNA editing at two sites in Physcomitrella patens. Plant Cell Physiol. 58, 496–507. https://doi.org/10.1093/pcp/pcw229.
Schertl, P., Braun, H.-P., 2014. Respiratory electron transfer pathways in plant mitochondria. Front. Plant Sci. 5, 163. https://doi.org/10.3389/fpls.2014.00163.
Sechet, J., Roux, C., Plessis, A., Effroy, D., Frey, A., Perreau, F., Biniek, C., Krieger-Liszkay, A., Macherel, D., North, H.M., Mireau, H., Marion-Poll, A., 2015. The ABA-deficiency suppressor locus HAS2 encodes the PPR protein LOI1/MEF11 involved in mitochondrial RNA editing. Mol. Plant 8, 644–656. https://doi.org/10.1016/J.MOLP.2014.12.005.
Senkler, J., Rugen, N., Eubel, H., Hegermann, J., Braun, H.-P., 2018. Absence of complex I implicates rearrangement of the respiratory chain in european mistletoe. Curr. Biol. 28, 1606–1613. https://doi.org/10.1016/j.cub.2018.03.050. e4.
Shi, X., Hanson, M.R., Bentolila, S., 2015. Two RNA recognition motif-containing proteins are plant mitochondrial editing factors. Nucleic Acids Res. 43, 3814–3825. https://doi.org/10.1093/nar/gkv245.
Shikanai, T., Fujii, S., 2013. Function of PPR proteins in plastid gene expression. RNA Biol. 10, 1446–1456. https://doi.org/10.4161/rna.25207.
Sosso, D., Mbelo, S., Vernoud, V., Gendrot, G., Dedieu, A., Chambrier, P., Dauzat, M., Heurtevin, L., Guyon, V., Takenaka, M., Rogowsky, P.M., 2012. PPR2263, a DYW-Subgroup Pentatricopeptide repeat protein, is required for mitochondrial nad5 and cob transcript editing, mitochondrion biogenesis, and maize growth. Plant Cell 24, 676–691. https://doi.org/10.1105/tpc.111.091074.
Sultan, L.D., Mileshina, D., Grewe, F., Rolle, K., Abudraham, S., Głodowicz, P., Niazi, A.K., Keren, I., Shevtsov, S., Klipcan, L., Barciszewski, J., Mower, J.P., Dietrich, A., Ostersetzer-Biran, O., 2016. The reverse transcriptase/RNA maturase protein MatR is required for the splicing of various group II introns in Brassicaceae mitochondria. Plant Cell 28, 2805–2829. https://doi.org/10.1105/tpc.16.00398.
Sun, T., Germain, A., Giloteaux, L., Hammani, K., Barkan, A., Hanson, M.R., Bentolila, S., 2013. An RNA recognition motif-containing protein is required for plastid RNA editing in Arabidopsis and maize. Proc. Natl. Acad. Sci. U. S. A 110, E1169–E1178. https://doi.org/10.1073/pnas.1220162110.
Sun, F., Wang, X., Bonnard, G., Shen, Y., Xiu, Z., Li, X., Gao, D., Zhang, Z., Tan, B.C., 2015. Empty pericarp7 encodes a mitochondrial E-subgroup pentatricopeptide repeat protein that is required for ccmFNediting, mitochondrial function and seed development in maize. Plant J. 84, 283–295. https://doi.org/10.1111/tpj.12993.
Sun, T., Bentolila, S., Hanson, M.R., 2016. The unexpected diversity of plant organelle RNA editosomes. Trends Plant Sci. 21, 962–973. https://doi.org/10.1016/j.tplants.2016.07.005.
Sung, T.Y., Tseng, C.C., Hsieh, M.H., 2010. The SLO1 PPR protein is required for RNA editing at multiple sites with similar upstream sequences in Arabidopsis mitochondria. Plant J. 63, 499–511. https://doi.org/10.1111/j.1365-313X.2010.04258.x.
Takenaka, M., 2010. MEF9, an E-subclass pentatricopeptide repeat protein, is required for an RNA editing event in the nad7 transcript in mitochondria of Arabidopsis. Plant Physiol. 152, 939–947. https://doi.org/10.1104/pp.109.151175.
Takenaka, M., Verbitskiy, D., Zehrmann, A., Brennicke, A., 2010. Reverse genetic screening identifies five E-class PPR proteins involved in RNA editing in mitochondria of Arabidopsis thaliana. J. Biol. Chem. 285https://doi.org/10.1074/jbc.M110.128611. 27122–9.
Takenaka, M., Zehrmann, A., Verbitskiy, D., Kugelmann, M., Härtel, B., Brennicke, A., 2012. Multiple organellar RNA editing factor (MORF) family proteins are required for RNA editing in mitochondria and plastids of plants. Proc. Natl. Acad. Sci. U. S. A 109, 5104–5109. https://doi.org/10.1073/pnas.1202452109.
Takenaka, M., Zehrmann, A., Verbitskiy, D., Härtel, B., Brennicke, A., 2013a. RNA editing in plants and its evolution. Annu. Rev. Genet. 47, 335–352. https://doi.org/10.1146/annurev-genet-111212-133519.
Takenaka, M., Zehrmann, A., Brennicke, A., Graichen, K., 2013b. Improved computational target site prediction for pentatricopeptide repeat RNA editing factors. PLoS One 8, e65343. https://doi.org/10.1371/journal.pone.0065343.
M. Takenaka, D. Verbitskiy, A. Zehrmann, A. Brennicke, Reverse Genetic Screening Identifies PPR-proteins Required for Different RNA Editing Sites in Mitochondria of Arabidopsis thaliana : at Least Ten Percent of the E-class PPR Proteins Are Involved in Non-essential Mitochondrial Editing Events, (n.d.).
Tasaki, E., Hattori, M., Sugita, M., 2010. The moss pentatricopeptide repeat protein with a DYW domain is responsible for RNA editing of mitochondrial ccmFc transcript. Plant J. 62, 560–570. https://doi.org/10.1111/j.1365-313X.2010.04175.x.
Tillich, M., Hardel, S.L., Kupsch, C., Armbruster, U., Delannoy, E., Gualberto, J.M., Lehwark, P., Leister, D., Small, I.D., Schmitz-Linneweber, C., 2009. Chloroplast ribonucleoprotein CP31A is required for editing and stability of specific chloroplast mRNAs. Proc. Natl. Acad. Sci. U. S. A 106, 6002–6007. https://doi.org/10.1073/pnas.0808529106.
Toda, T., Fujii, S., Noguchi, K., Kazama, T., Toriyama, K., 2012. Rice *MPR25* encodes a pentatricopeptide repeat protein and is essential for RNA editing of *nad5* transcripts in mitochondria. Plant J. 72, 450–460. https://doi.org/10.1111/j.1365-313X.2012.05091.x.
Uchida, M., Ohtani, S., Ichinose, M., Sugita, C., Sugita, M., 2011. The PPR-DYW proteins are required for RNA editing of *rps14* , *cox1* and *nad5* transcripts in *Physcomitrella patens* mitochondria. FEBS Lett. 585, 2367–2371. https://doi.org/10.1016/j.febslet.2011.06.009.
Unseld, M., Marienfeld, J.R., Brandt, P., Brennicke, A., 1997. The mitochondrial genome of Arabidopsis thaliana contains 57 genes in 366,924 nucleotides. Nat. Genet. 15, 57–61. https://doi.org/10.1038/ng0197-57.
Verbitskiy, D., Zehrmann, A., Van Der Merwe, J.A., Brennicke, A., Takenaka, M., 2010.

The PPR protein encoded by the lovastatin insensitive 1 gene is involved in RNA editing at three sites in mitochondria of Arabidopsis thaliana. Plant J. 61. https://doi.org/10.1111/j.1365-313X.2009.04076.x.

Verbitskiy, D., Härtel, B., Zehrmann, A., Brennicke, A., Takenaka, M., 2011. The DYW-E-PPR protein MEF14 is required for RNA editing at site matR-1895 in mitochondria of Arabidopsis thaliana. FEBS Lett. 585, 700–704. https://doi.org/10.1016/j.febslet.2011.01.037.

Verbitskiy, D., Zehrmann, a., Hartel, B., Brennicke, a., Takenaka, M., 2012a. Two related RNA-editing proteins target the same sites in mitochondria of Arabidopsis thaliana. J. Biol. Chem. 287, 38064–38072. https://doi.org/10.1074/jbc.M112.397992.

Verbitskiy, D., van der Merwe, J.A., Zehrmann, A., Härtel, B., Takenaka, M., 2012b. The E-class PPR protein MEF3 of Arabidopsis thaliana can also function in mitochondrial RNA editing with an additional DYW domain. Plant Cell Physiol. 53, 358–367. https://doi.org/10.1093/pcp/pcr182.

Wang, G., Zhong, M., Shuai, B., Song, J., Zhang, J., Han, L., Ling, H., Tang, Y., Wang, G., Song, R., 2017. E+ subgroup PPR protein defective kernel 36 is required for multiple mitochondrial transcripts editing and seed development in maize and Arabidopsis. New Phytol. 214, 1563–1578. https://doi.org/10.1111/nph.14507.

Weiner, J.H., Bilous, P.T., Shaw, G.M., Lubitz, S.P., Frost, L., Thomas, G.H., Cole, J.A., Turner, R.J., 1998. A novel and ubiquitous system for membrane targeting and secretion of cofactor-containing proteins. Cell 93, 93–101. https://doi.org/10.1016/S0092-8674(00)81149-6.

Weißenberger, S., Soll, J., Carrie, C., 2017. The PPR protein SLOW GROWTH 4 is involved in editing of nad4 and affects the splicing of nad2 intron 1. Plant Mol. Biol. 93, 355–368. https://doi.org/10.1007/s11103-016-0566-4.

Xiao, H., Zhang, Q., Qin, X., Xu, Y., Ni, C., Huang, J., Zhu, L., Zhong, F., Liu, W., Yao, G., Zhu, Y., Hu, J., 2018a. Rice PPS1 encodes a DYW motif-containing pentatricopeptide repeat protein required for five consecutive RNA-editing sites of nad3 in mitochondria. New Phytol. https://doi.org/10.1111/nph.15347.

Xiao, H., Xu, Y., Ni, C., Zhang, Q., Zhong, F., Huang, J., Liu, W., Peng, L., Zhu, Y., Hu, J., 2018b. A rice dual-localized pentatricopeptide repeat protein is involved in organellar RNA editing together with OsMORFs. J. Exp. Bot. 69, 2923–2936. https://doi.org/10.1093/jxb/ery108.

Xie, T., Chen, D., Wu, J., Huang, X., Wang, Y., Tang, K., Li, J., Sun, M., Peng, X., 2016. Growing Slowly 1 locus encodes a PLS-type PPR protein required for RNA editing and plant development in Arabidopsis. J. Exp. Bot. 67, 5687–5698. https://doi.org/10.1093/jxb/erw331.

Yagi, Y., Hayashi, S., Kobayashi, K., Hirayama, T., Nakamura, T., 2013. Elucidation of the RNA recognition code for pentatricopeptide repeat proteins involved in organelle RNA editing in plants. PLoS One 8, e57286. https://doi.org/10.1371/journal.pone.0057286.

Yan, J., Zhang, Q., Guan, Z., Wang, Q., Li, L., Ruan, F., Lin, R., Zou, T., Yin, P., 2017. MORF9 increases the RNA-binding activity of PLS-type pentatricopeptide repeat protein in plastid RNA editing. Native Plants 3. https://doi.org/10.1038/nplants.2017.37.

Yang, Y.Z., Ding, S., Wang, H.C., Sun, F., Huang, W.L., Song, S., Xu, C., Tan, B.C., 2017. The pentatricopeptide repeat protein EMP9 is required for mitochondrial ccmB and rps4 transcript editing, mitochondrial complex biogenesis and seed development in maize. New Phytol. 214, 782–795. https://doi.org/10.1111/nph.14424.

Yap, A., Kindgren, P., Colas Des Francs-Small, C., Kazama, T., Tanz, S.K., Toriyama, K., Small, I., 2015. AEF1/MPR25 is implicated in RNA editing of plastid atpF and mitochondrial nad5, and also promotes atpF splicing in Arabidopsis and rice. Plant J. 81, 661–669.

Yuan, H., Liu, D., 2012. Functional disruption of the pentatricopeptide protein SLG1 affects mitochondrial RNA editing, plant development, and responses to abiotic stresses in Arabidopsis. Plant J. 70, 432–444. https://doi.org/10.1111/j.1365-313X.2011.04883.x.

Yura, K., Go, M., 2008. Correlation between amino acid residues converted by RNA editing and functional residues in protein three-dimensional structures in plant organelles. BMC Plant Biol. 8, 1. https://doi.org/10.1186/1471-2229-8-79.

Yura, K., Sulaiman, S., Hatta, Y., Shionyu, M., Go, M., 2009. RESOPS: a database for analyzing the correspondence of RNA editing sites to protein three-dimensional structures. Plant Cell Physiol. 50, 1865–1873. https://doi.org/10.1093/pcp/pcp132.

Zehrmann, A., Verbitskiy, D., a van der Merwe, J., Brennicke, A., Takenaka, M., 2009. A DYW domain-containing pentatricopeptide repeat protein is required for RNA editing at multiple sites in mitochondria of Arabidopsis thaliana. Plant Cell 21, 558–567. https://doi.org/10.1105/tpc.108.064535.

Zehrmann, A., van der Merwe, J. a., Verbitskiy, D., Härtel, B., Brennicke, A., Takenaka, M., 2012. The DYW-class PPR protein MEF7 is required for RNA editing at four sites in mitochondria of *Arabidopsis thaliana*. RNA Biol. 9, 155–161. https://doi.org/10.4161/rna.18644.

Zehrmann, A., Härtel, B., Glass, F., Bayer-Császár, E., Obata, T., Meyer, E., Brennicke, A., Takenaka, M., 2015. Selective homo- and heteromer interactions between the multiple organellar RNA editing factor (MORF) proteins in Arabidopsis thaliana. J. Biol. Chem. 290, 6445–6456. https://doi.org/10.1074/jbc.M114.602086.

Zhang, F., Tang, W., Hedtke, B., Zhong, L., Liu, L., Peng, L., Lu, C., Grimm, B., Lin, R., 2014. Tetrapyrrole biosynthetic enzyme protoporphyrinogen IX oxidase 1 is required for plastid RNA editing. Proc. Natl. Acad. Sci. Unit. States Am. 111, 2023–2028. https://doi.org/10.1073/pnas.1316183111.

Zhou, W., Cheng, Y., Yap, A., Chateigner-Boutin, A.-L., Delannoy, E., Hammani, K., Small, I., Huang, J., 2008. The Arabidopsis gene YS1 encoding a DYW protein is required for editing of rpoB transcripts and the rapid development of chloroplasts during early growth. Plant J. 1–15. https://doi.org/10.1111/j.1365-313X.2008.03766.x.

Zhu, Q., Dugardeyn, J., Zhang, C., Takenaka, M., Kühn, K., Craddock, C., Smalle, J., Karampelias, M., Denecke, J., Peters, J., Gerats, T., Brennicke, A., Eastmond, P., Meyer, E.H.E.H., Van Der Straeten, D., Kuhn, K., Craddock, C., Smalle, J., Karampelias, M., Denecke, J., Peters, J., Gerats, T., Brennicke, A., Eastmond, P., Meyer, E.H.E.H., Van Der, S.D., 2012. SLO2, a mitochondrial pentatricopeptide repeat protein affecting several RNA editing sites, is required for energy metabolism. Plant J. 71, 836–849. https://doi.org/10.1111/j.1365-313X.2012.05036.x.