GENE CLUSTERS FOR BIOSYNTHESIS OF MYCOSPORINE-LIKE AMINO ACIDS IN DINOFLAGELLATE NUCLEAR GENOMES: POSSIBLE RECENT HORIZONTAL GENE TRANSFER BETWEEN SPECIES OF SYMBIODINIACEAE (DINOPHYCEAE)¹

Eiichi Shoguchi ²

Marine Genomics Unit, Okinawa Institute of Science and Technology Graduate University, Onna, Okinawa 904-0495, Japan

Global warming increases the temperature of the ocean surface, which can disrupt dinoflagellate-coral symbioses and result in coral bleaching. Photosynthetic dinoflagellates of the family Symbiodiniaceae include bleaching-tolerant and bleaching-sensitive coral symbionts. Therefore, understanding the molecular mechanisms for changing symbiont diversity is potentially useful to assist recovery of coral holobionts (corals and their associated microbes, including multiple species of Symbiodiniaceae), although sexual reproduction has not been observed in the Symbiodiniaceae. Recent molecular phylogenetic analyses estimate that the Symbiodiniaceae appeared 160 million years ago and diversified into 15 groups, five genera of which now have available draft genomes (i.e., Symbiodinium, Durusdinium, Breviolum, Fugacium, and Cladocopium). Comparative genomic analyses have suggested that crown groups have fewer gene families than early-diverging groups, although many genes that were probably acquired via gene duplications and horizontal gene transfers (HGTs) have been found in each decoded genome. Because UV stress is likely a contributor to coral bleaching, and because the highly conserved gene cluster for mycosporine-like amino acid (MAA) biosynthesis has been found in thermal-tolerant symbiont genomes, I reviewed genomic features of the Symbiodiniaceae, focusing on possible acquisition of a biosynthetic gene cluster for MAAs, which absorb UV radiation. On the basis of highly conserved noncoding sequences, I hypothesized that HGTs have occurred among members of the Symbiodiniaceae and have contributed to the diversification of Symbiodiniaceae–host relationships. Finally, I proposed that bleaching tolerance may be strengthened by multiple MAAs from both symbiotic dinoflagellates and corals.

Key index words: Symbiodiniaceae genomes; gene cluster; horizontal gene transfer; Symbiodiniaceae–Symbiodiniaceae interactions; diversified MAAs; coral bleaching; Symbiodinium; Durusdinium; gene expression regulation

Abbreviations: GMC oxidoreductase, glucose-methanol-choline oxidoreductase; HGT, horizontal gene transfer; MAAs, mycosporine-like amino acids

Symbiotic dinoflagellates of the family Symbiodiniaceae are well-known photosynthetic partners of corals and other nonphotosynthetic hosts in subtropical and tropical shallow waters, where they comprise essential components of coral reef ecosystems (Coffroth and Santos 2005, Brodie et al. 2017, LaJeunesse et al. 2018). Using molecular phylogenetic analyses, the family Symbiodiniaceae (previously the genus Symbiodinium) has been classified into 15 major groups, of which 11 were assigned to that genus (Fig. 1a; LaJeunesse et al. 2018, Nitschke et al. 2020, LaJeunesse et al. 2011, Pochon and LaJeunesse 2021). Members of the Symbiodiniaceae are hosted by ciliates, foraminifers, sponges, cnidarians, acoels, and mollusks (Hikosaka-Katayama et al. 2012, Pochon et al. 2014, LaJeunesse et al. 2018, Mies 2019). Although many Symbiodiniaceae–host relationships and some free-living Symbiodiniaceae have been reported (Fig. 1a; Carlos et al. 1999, Hirose et al. 2008, Yamashita and Koike 2013, Fujise et al. 2021), recent molecular-level studies have focused on symbiotic relationships between symbiotic dinoflagellates and corals (Davy et al. 2012, Cunning and Baker 2013, McIlroy and Coffroth 2017, Reich et al. 2017, González-Pech et al. 2019). In this era of rapid global climate change, disruption of these relationships has resulted in coral bleaching (Smith et al. 2005) and subsequent coral mortality, leading to discussions of coral reef recovery (Loya et al. 2001, Baker et al. 2008, Dixon et al. 2015, Prada et al. 2016).

Collapsed symbioses between host corals and their dinoflagellate symbionts are due to rapid changes
in temperature and insolation, especially UV radiation (Lesser et al. 1990, Warner et al. 1999, Loya et al. 2001, Rowan 2004). As global warming progresses, it is predicted that coral bleaching will occur more frequently (Hughes et al. 2018). Coral transplantation and other attempts at coral
Fig. 1. Known symbiotic connections between dinoflagellates of the family Symbiodiniaceae and hosts. (a) Left shows 15 groups of Symbiodiniaceae (Lajeunesse et al. 2018). The inset image is Symbiodinium tridacnidorum Y106 (NIES-4076), showing two flagella (arrowheads), the genome of which has a gene cluster for mycosporine-like amino acid (MAA) biosynthesis. Right indicates hosts for Symbiodiniaceae. Dashed lines show Symbiodiniaceae-host connections that have been reported. Genera of the Symbiodiniaceae with two asterisks (**) include a sequenced genome that has a MAA biosynthetic gene cluster. The blue arrow between Symbiodinium and Durusdinium indicates the possibility that the MAA biosynthetic gene cluster may have been shared via a recent horizontal gene transfer. Clado- copium, Fugacium, and Breviolum with asterisks (*) have some MAA biosynthetic genes that are probably not clustered (Liu et al. 2018). Host cnidarians with asterisks (*) include corals and sea anemones that have MAA biosynthetic genes (Shinzato et al. 2011, Baumgarten et al. 2015). Red branches show the lineage of unicellular eukaryotes that may have participated in a red algal secondary endosymbiotic event (Bhattacharya et al. 2004). (b) A hypothesis for changing from bleaching-sensitive holobionts to bleaching-tolerant holobionts with thermally tolerant symbionts having a recently acquired MAA biosynthetic gene cluster. An illustration of a hypothesis explaining why Durusdinium likely contributes to bleaching resistance of corals, even though the means by which Symbiodiniaceae populations in corals respond to climate change is little known. Left shows that Durusdinium is a minor component in Symbiodiniaceae-host relationships. Major Symbiodiniaceae that lack MAA biosynthetic gene clusters may contribute to fast-growing corals (van Oppen and Medina 2020). In the right illustration, Durusdinium, with the MAA biosynthetic gene cluster, may enable coral holobionts to become bleaching-tolerant (Hidaka 2016).

NUCLEAR GENOMIC FEATURES OF SYMBIOTIC DINOFLAGELLATES

Unusual nuclear features of dinoflagellates include large genome sizes and permanently condensed chromosomes (Wong 2019). Most core dinoflagellate genomes have genomes larger than the human genome (3 Gbp; Janouškovec et al. 2017, Beedessee et al. 2020). However, some Symbiodiniaceae are thought to have smaller genomes (Lajeunesse et al. 2005, Saad et al. 2020). Transcriptomes of Symbiodiniaceae have been analyzed (Leggat et al. 2007, 2011, Bayer et al. 2012) and draft genomes of 15 strains from five genera have been published (Shoguchi et al. 2013, 2018, 2021, Lin et al. 2015, Aranda et al. 2016, Liu et al. 2018, Li et al. 2020, González-Pech et al. 2021, Yoshioka et al. 2021). Those genomes clarified unusual gene structures and revealed many repetitive sequences (both coding and noncoding) with unknown functions, suggesting a high frequency of gene duplications. Expanded sequences include transposons, transporter genes, and repeat domain-containing genes, such as leucine-rich repeats and retroviral-related dUTPsases (Lin et al. 2015, Aranda et al. 2016, Shoguchi et al. 2018). Symbiodiniaceae genomes include many bacteria-like genes (Leggat et al. 2007, Shoguchi et al. 2013), implying frequent HGTs (Fan et al. 2020). Thus far, gene family numbers in Symbiodiniaceae genomes are larger than in genomes of other major alveolates, ciliates, and apicomplexans (Shoguchi et al. 2013). Genomes in Symbiodinium, which is an early-diverging sister to the other Symbiodiniaceae lineages, likely have more gene families than genomes of crown Clado- copium, although some Symbiodinium species may have fewer gene families (Shoguchi et al. 2018, González-Pech et al. 2021). In addition to Symbiodiniaceae genomes, other recent core dinoflagellate genomes (Beedessee et al. 2020, Stephens et al. 2020) confirm that dinoflagellate genomes with complex exon-intron structures are unidirectionally arranged, suggesting poly- cancistrionic expression with spliced leader trans- splicing (Zhang et al. 2007). Comparative analysis of

coronation and restoration have been performed (West and Salm 2003, Baums 2008, Shinzato et al. 2014b, Zayas et al. 2018). Thermally tolerant coral symbionts may be important for coral conservation (Stat and Gates 2010). For example, different responses to heat stress have been observed using cultured symbiont cells (Reynolds et al. 2008, Takahashi et al. 2008, van Oppen et al. 2009, Aihara et al. 2016, Reich et al. 2021). Transplantation experiments with corals indicate that the Durusdinium group includes species that are more resistant to bleaching (Berkelmans and van Oppen 2006, Stat and Gates 2010). However, how the algae achieve enhanced resistance to bleaching within host corals is unknown (Ladner et al. 2012).

One strategy by which coral holobionts resist UV stress is production of water-soluble molecules that absorb UV radiation, known as mycosporine-like amino acids (MAAs; Shibata 1969, Shick and Dunlap 2002). However, it is unclear which of the symbiotic partners produce MAAs, because genes and enzymes for their biosynthesis were not identified until about 10 years ago. The MAA biosynthetic gene cluster was first identified in cyanobacteria by Balskus and Walsh (2010), and the decoded genome of the coral, Acropora digitifera, revealed that homologs of MAA biosynthetic genes are encoded in the genomes of host corals (Fig. 1; Shinzato et al. 2011). After that, draft Symbiodiniaceae genomes were reported and predicted genes were discussed (Shoguchi et al. 2013, 2018, 2021, Lin et al. 2015, Aranda et al. 2016, Liu et al. 2018, Robbins et al. 2019, Chen et al. 2020, González-Pech et al. 2021, Yoshioka et al. 2021). We identified the MAA biosynthetic cluster in genomes of the symbiotic dinoflagellates, Symbiodinium tridacnidorum and Durusdinium trenchii. In this mini-review, I briefly describe genomic features of these dinoflagellates and explain the gene cluster regions involved in MAA biosynthesis. For future studies, I hypothesize the possibility of horizontal gene transfers (HGTs) of these clusters between dinoflagellates and focus on a discussion of the importance of MAAs in bleaching resistance of coral holobionts.
Symbiodiniaceae genomes has also revealed higher GC content in *Symbiodinium* than in other Symbiodiniaceae lineages (Aranda et al. 2016, Shoguchi et al. 2018) and metabolic genes containing syntenic blocks (Liu et al. 2018). When metabolic genes acquire polycistronic expression that is likely similar to bacterial operons, higher expression levels may have been attained than is possible with monocistronic expression (Lim et al. 2011). However, such a conclusion is premature because relationships between polycistronic expression and expression regulation have yet to be determined in dinoflagellate genomes (Yang et al. 2020).

**MAA biosynthesis in Symbiodiniaceae-coral symbiosis**

In Symbiodiniaceae–host symbiosis, the significance of metabolic exchanges have been examined and discussed (Davy et al. 2012, Ip et al. 2020). Diversification and regulation of metabolic pathway genes in Symbiodiniaceae have likely involved specifying and maintaining symbioses with hosts (Lin et al. 2019). For example, it has been suggested that host MAAs may increase the amount of photosynthate released by the Symbiodiniaceae (Gates et al. 1995), but this has not been confirmed. On the other hand, different capacities to synthesize MAAs have been found among cultured *Symbiodinium* and other Symbiodiniaceae, including *Breviolum* and *Cladocopium* (Banaszak et al. 2000). These transparent, water-soluble compounds were first discovered in jellyfish (Wittenberg 1960) and then in red algae (Tsujino 1961) and corals (Shibata 1969). The role of MAAs as UV screens is well established, although other functions, such as antioxidation, have also been discussed for MAAs in the microbial world (Oren and Gunde-Cimerman 2007, Singh et al. 2008). MAA UV sunscreen activity has been examined in the dinoflagellate, *Gymnodinium sanguineum* (Neale et al. 1998). In dinoflagellates, *Alexandrium* and *Heterocapsa*, it is thought that MAAs may be concentrated around UV-sensitive organelles (Laurion et al. 2004); however, this has yet to be confirmed.

Fifteen MAAs have been identified in reef-building coral holobionts (Shick and Dunlap 2002, Rosic and Dove 2011). However, it remains unclear which organism produces these diverse MAAs, since genes and enzymes for their biosynthesis had not been identified in 2009. It has been reported that MAA concentrations in coral holobionts are higher when UV radiation is doubled, but the mechanism of regulation is unknown (Shick 2004). Although it has been hypothesized that MAAs are synthesized via the shikimate pathway (Shick et al. 1999), which includes a plastid-targeted fusion protein in dinoflagellates (Waller et al. 2006), this remains to be conclusively demonstrated (Cardozo et al. 2007).

The MAA biosynthetic gene cluster was first identified in a cyanobacterium and all four biosynthetic enzymes were characterized in vitro (Balskus and Walsh 2010). Dimethyl 4-deoxygadusol (DDG) synthase, O-methyl-transferase (O-MT), and ATP-grasp are conserved in the cyanobacterial gene cluster. The gene for the fourth biosynthetic step is either a nonribosomal peptide synthetase (NRPS) homolog or a D-alanine (D-Ala) D-Ala ligase homolog. Gene clusters have been also found in red algal genomes and four putative genes for MAA porphyra-334 are fused into two genes, DDG/O-MT and ATP-grasp/ D-Ala D-Ala ligase (Brawley et al. 2017). Five MAAs, mycosporine-glycine, mycosporine-2-glycine, shi- norine, palythine, and porphyra-334, have been identified in the Symbiodiniaceae (Banaszak et al. 2006, Rosic and Dove 2011). At that time, it was predicted that symbiotic algae synthesize the MAAs. However, draft genomes of corals suggest that MAAs are also produced by corals (Shinzato et al. 2011, Bhattacharya et al. 2016). Considering that 15 MAAs have been identified in coral holobionts, our understanding of the enzymatic and genetic basis of their synthesis is still limited. Many homologs for MAA biosynthetic genes have been also reported in transcriptomes of the Symbiodiniaceae (Silva Lima et al. 2020). Each of those genes may be involved in biosynthesis of various MAAs. Omics data and functional analyses will clarify diverse MAA biosynthetic pathways and their regulation (Meyer and Weis 2012).

**The MAA biosynthetic gene cluster in bleaching-tolerant species**

In prokaryotes, conserved MAA biosynthetic gene clusters have been identified (Balskus and Walsh 2010) and the gene cluster in eukaryotes was recently identified in the red alga, *Porphyra umbilicalis* (Brawley et al. 2017). In dinoflagellates, the draft genome of *Symbiodinium tridacnidorum* (previously *Symbiodinium* sp. clade A3) identified a gene cluster for enzymes involved in MAA biosynthesis (Shoguchi et al. 2018). The common characteristic of red algae and dinoflagellates was a possible fused protein with functions of both DDG synthase and O-MT (Waller et al. 2006). The fused protein is also predicted in genomes of sea anemones and corals, but evolutionary relationships and functions remain to be examined. Comparative analysis suggests that orthologs of these genes have been lost in the common ancestor of *Breviolum* and *Cladocopium*, although homologs for MAA biosynthetic genes have been described in genomic analyses of *C. gore-aui* (Liu et al. 2018). Other genes for UV-damage protection may exist in the *Breviolum* and *Cladocopium* genomes (Liu et al. 2018, Shoguchi et al. 2018). However, an alternative strategy among crown groups of Symbiodiniaceae likely utilizes sunscreen from the hosts, because some hosts, including sea anemones and corals, also have gene homologs for MAA biosynthetic genes (Fig. 2a). In
addition, cnidarians have diverse fluorescent proteins with photoprotective functions (Matz et al. 1999, Alieva et al. 2008, Smith et al. 2013, Satoh et al. 2020, Kashimoto et al. 2021). Thus, it is possible to speculate that late-diverging groups, Breviolum and Cladocopium, require hosts such as cnidarians to receive adequate insolation. Genome evolution of the Symbiodiniaceae has been discussed (González-Pech et al. 2019). The loss of gene families for metabolic pathway genes may contribute to the transition from free-living to putative obligate symbionts (Shoguchi et al. 2018, González-Pech et al. 2019).

On the other hand, the draft assembly of Durusdinium trenchii, which occupies an intermediate phylogenetic position, contains a gene cluster for MAA biosynthesis, expression of which is supported by transcriptomic data (Shoguchi et al. 2021; Fig. 2b). Moreover, the gene order is conserved between Symbiodinium tridacnidorum and D. trenchii. Additionally, we found that the neighboring gene to ATP-grasp on the 3’-end of the cluster encodes an enzyme resembling a member of the GMC (glucose-methanol-choline) oxidoreductase family. This homolog also occurs in the genome of S. tridacnidorum and is located adjacent to the MAA gene cluster (Fig. 2), indicating syntenic conservation of metabolic genes among members of the Symbiodiniaceae (Liu et al. 2018). It has been suggested that GMC oxidoreductase with FAD may change enzyme activity by altering light intensity (Shoguchi et al. 2021), but it remains unknown whether this GMC oxidoreductase functions in MAA biosynthesis. As far as I am aware, the MAA-GMC gene cluster has not been studied in cyanobacteria and other organisms (Singh et al. 2010). Functions of proteins and regulatory mechanisms in MAA biosynthesis with potentially polycistronic and alternative mRNAs will be clarified by heterologous expression analysis.

**POSSIBLE RECENT HORIZONTAL TRANSFERS OF MAA BIOSYNTHETIC GENES AMONG TAXA OF THE SYMBIODINIACEAE**

Predicted fusions of DDG synthase and O-MT suggest that dinoflagellates obtained the fused gene from a red alga through secondary endosymbiosis (Waller et al. 2006, Brawley et al. 2017). The DDG synthase of Symbiodinium tridacnidorum Y106 may also have been transferred from a red alga, according to molecular phylogenetic analysis (Shoguchi et al. 2018; Fig. 2a). On the other hand, molecular phylogenetics for the GMC oxidoreductase of the Symbiodiniaceae found that evolutionary relationships remain uncertain (Shoguchi et al. 2021). Therefore, I cannot exclude the possibility that the MAA-GMC cluster formed in the Symbiodiniaceae lineage. For example, sequences similar to reverse transcriptases, related to retroviruses or retrotransposons, were found ~9 kbp downstream of the MAA-GMC cluster in S. tridacnidorum, suggesting the involvement of transposition mechanisms. Since Symbiodiniaceae genomes have repeated transposon sequences (Song et al. 2017), understanding formation of this cluster is likely to be an interesting research topic in dinoflagellate genome evolution (Hou et al. 2019).

Durusdinium trenchii NIES-2907 genome sequences imply putative conservation of the MAA-GMC cluster (genes for D-Ala D-Ala ligase, DDG synthase, O-MT, ATP-grasp, and GMC oxidoreductase) between Symbiodinium tridacnidorum and D. trenchii (Shoguchi et al. 2021). Available transcriptomic data from other Symbiodiniaceae strains (Keeling et al. 2014, Yu et al. 2020) suggest that S. tridacnidorum CCMP2430 (transcriptome assemblies: MMETSP1115, MMETSP1116, and MMETSP1117) and D. trenchii (transcriptome assembly: MMETSP1377) have highly conserved genes for D-Ala D-Ala ligase, DDG synthase, O-MT, ATP-grasp, and GMC oxidoreductase (data not shown). The possibility of cross-contamination in laboratory cultures may be discussed when genomes of those strains with transcriptomic information are decoded in the future. Curiously, pairwise alignments of MAA-GMC clusters include intron and intergenic sequences with 100% matches between S. tridacnidorum (scaffold 314) and D. trenchii (scaffold 2498). MAA-GMC cluster regions, including introns and intergenic sequences, are highly conserved between Symbiodinium and Durusdinium. Sequence similarities of ~20 kb were ~99%, except for the third intron of D-Ala D-Ala ligase. The third intron of D-Ala D-Ala ligase had an insert of ~4 kb in D. trenchii. The only D-Ala D-Ala ligase has typical exon-intron structure, in contrast to other genes with long exons (Fig. 2b).

On the other hand, an alignment of S. tridacnidorum scaffold 4185 and D. trenchii scaffold 331, which contains a microsyntenic region, including genes from secondary endosymbiosis, showed less than 80% similarity of gacU (Rho GTPase-activating protein) and psaE (Photosystem I reaction center subunit IV; Hackett et al. 2004, Mungpakdee et al. 2014). Apparent homology of exons was confirmed (Fig. 2c), corresponding to comparative analyses of transcriptomes with 72.7–81.5% similarity (Ladner et al. 2012). Therefore, it is difficult to explain sequence conservation of MAA biosynthetic gene regions during the ~160 my since their divergence. I hypothesize that HGTs of the gene cluster may have occurred among Symbiodiniaceae species, although more evidence for it is required (Fig. 1a). If there were no HGT events among Symbiodiniaceae species, how have conserved sequences, which include noncoding sequences (introns and intergenic sequences) been maintained in both lineages? To find the conserved MAA-GMC cluster, the genome of the other S. tridacnidorum CCMP2592 from the Great Barrier Reef (GBR) and the other Symbiodinium genomes (González-Pech et al. 2021, Yoshioka et al. 2021) were surveyed, but the cluster was not detected (data not shown). This supports the genomic structural divergences that
have been reported in the genus *Symbiodinium* (González-Pech et al. 2021). In the case of *S. tridacnidorum* and *D. trenchii* (Shoguchi et al. 2018, 2021), both strains are from Okinawa, Japan, suggesting that detailed synteny analysis of Symbiodiniaceae genomes from the same habitats may detect additional highly conserved noncoding sequences (>200 bp), which could be defined as ultraconserved elements (100% identity with no insertions or deletions; Bejerano et al. 2004). On the other hand, this hypothesis does not exclude the possibility of convergent evolution, because the highly conserved intragenic and intergenic regions may be important for regulation or efficient transcription of clustered genes. High-quality genomes likely will detect sequences for increasing numbers of HGT events (Van Etten and Bhattacharya 2020, Marinov et al. 2021, Nand et al. 2021) and ultraconserved elements. Both *S. tridacnidorum* Y106 and *D. trenchii* NIES-2907 have been found in the same habitat (Shoguchi et al. 2018, 2021), implying possible HGT. Thus, Symbiodiniaceae–Symbiodiniaceae interactions will be also investigated in holobiont genome analyses (Matthews et al. 2020, McLroy et al. 2020), in addition to Symbiodiniaceae–bacteria connections (Garrido et al. 2020). Furthermore, it remains to be seen whether HT genes in dinoflagellates depend on mechanisms similar to those of bacteria (Thomas and Nielsen 2005, McDaniel et al. 2010, Lang et al. 2012, Soucy et al. 2015) or associated viruses (Correa et al. 2013). For examples of possible HT genes, a Form II RuBisCO from proteobacteria and DVNP (dinoflagellate/viral nucleoproteins) from an algal virus have been reported in dinoflagellates (Morse et al. 1995, Gornik et al. 2012, Janouškové et al. 2017). HGTs may be more common in cases of reduced adaptability when the capacity for sexual reproduction is reduced (Brian et al. 2019, Shah et al. 2020).

**PERSPECTIVES**

Draft genomes from the Symbiodiniaceae have revealed many unusual gene structures in their nuclear genome sequences that are complicated by an abundance of duplicate genes, spliceosomal introns, and transposable elements (Lynch and Conery 2003). When findings of MAA biosynthetic clusters in Symbiodiniaceae genomes were reviewed, one question was whether acquisition of the MAA biosynthetic gene cluster by the Symbiodiniaceae lineage led to higher bleaching resistance. In addition, it remains unexamined whether clustered gene structures in dinoflagellate genomes enhance their transcriptional efficiency (Stephens et al. 2020). The MAA-GMC gene cluster has been found only in two genomes in the Symbiodiniaceae, probably due to sampling bias in genome sequencing. Since sunlight intensity in seawater is important for survival in coral reefs, multiple tools to cope with it have likely evolved in symbiotic dinoflagellates (Maruyama et al. 2015, Shimakawa et al. 2021). Little is known about how symbioses between corals and Symbiodiniaceae populations respond to dramatic climate shifts, but trade-offs between fast growth and thermal tolerance have been discussed (van Oppen and Medina 2020). If both hosts and dinoflagellates can produce MAAs, coral holobionts, including potentially opportunistic or parasitic *Durusdinium* may have become more adaptable (LaJeunesse et al. 2009, Lesser et al. 2013).

I propose that a gene cluster for MAA biosynthesis in Symbiodiniaceae genomes may function as a tool for bleaching resistance, if diversification of the capacity for MAA biosynthesis partially contributes to maintenance of symbiotic relationships in response to UV stress (Fig. 1b). To test this hypothesis, the mechanism of HGT will be explored by functional analyses of sequences adjoining the conserved MAA-GMC cluster. If HGTs between Symbiodiniaceae genomes can be induced in the lab, possible gene sets for bleaching resistance may be validated in the near future. It has been reported that *Symbiodinium* (ITS type: A3) and *Durusdinium* (ITS type: D1a) increased during rapid recovery from bleaching in the Caribbean (Kemp et al. 2014). During recovery, possible gene sequences for bleaching resistance may be detected in environmental DNA. Other thermally tolerant species have been reported in addition to possible bleaching-tolerant symbionts (Swain et al. 2017, Ziegler et al. 2017, LaJeunesse et al. 2018). Those include GBR.
populations of the general Cladocinium (ITS type: C1; Howells et al. 2011, Levin et al. 2016) and Cladocinium thermophilum (C3gulf) in the Persian Gulf (Hune et al. 2016, Howells et al. 2020). Have any of those populations acquired functional genes via HGTs or epigenetic changes that are involved in thermal tolerance? It remains to be seen whether the ability to synthesize MAAs has increased in thermally tolerant species. Biosynthesis of other metabolites and gene functions that I did not review may prove more important than MAA biosynthesis for bleaching resistance (Bellantuono et al. 2019, Poquita-Du et al. 2020, Yuyama et al. 2021). Omics resources with major-minor symbiont interactions will likely provide further insights into the relationship between symbionts and hosts (Weber and Medina 2012, Shinzato et al. 2014a, Weis 2019, González-Pech et al. 2021, Williams et al. 2021).

I gratefully acknowledge Nori Satoh for his encouragement in preparing this manuscript and Steven D. Aird for editing and helpful comments. I appreciate all members of Marine Genomics Unit in OIST for their kind support. This work was supported by the Japan Society for the Promotion of Science (No. 20K05798 to ES.).

E. Shoguchi: Conceptualization (lead); Funding acquisition (lead); Resources (lead); Supervision (lead); Visualization (lead); Writing-original draft (lead); Writing-review & editing (lead).

AUTHOR CONTRIBUTION

Aihära, Y., Takahashi, S. & Minagawa, J. 2016. Heat induction of cyclic electron flow around photosystem I in the symbiotic dinoflagellate Symbiodinium. Plant Physiol. 171:522–9.

Alieva, N. O., Konzen, K. A., Field, S. F., Meleshkevitch, E. A., Hunt, M. E., Beltran-Ramirez, V., Miller, D. J., Wiedenmann, J., Salih, A. & Matz, M. V. 2008. Diversity and evolution of coral fluorescent proteins. PLoS ONE 3:e2680.

Aranda, M., Li, Y., Liew, Y. J., Baumgarten, S., Simakov, O., Wilson, M. C., Piel, J. et al. 2016. Genomes of coral dinoflagellate symbionts highlight evolutionary adaptations conducive to a symbiotic lifestyle. Sci. Rep. 6:39734.

Baker, A. C., Glynn, P. W. & Riegl, B. 2008. Climate change and coral reef bleaching: An ecological assessment of long-term impacts, recovery trends and future outlook. Estuar. Coast. Shelf Sci. 80:435–71.

Balaskus, E. P. & Walsh, C. T. 2010. The genetic and molecular basis for sunscreen biosynthesis in cyanobacteria. Science 329:1655–6.

Banaszak, A. T., Barba Santos, M. G., LaJeunesse, T. C. & Lesser, M. P. 2006. The distribution of mycosporine-like amino acids (MAAs) and the phylogenetic identity of symbiotic dinoflagellates in cnidarian hosts from the Mexican Caribbean. J. Exp. Mar. Bio. Ecol. 337:131–46.

Banaszak, A. T., LaJeunesse, T. C. & Trench, R. K. 2000. The synthesis of mycosporine-like amino acids (MAAs) by cultured, symbiotic dinoflagellates. J. Exp. Mar. Bio. Ecol. 249:219–33.

Baumgarten, S., Simakov, O., Eshrick, L. Y., Liew, Y. J., Lehner, E. M., Michell, C. T., Li, Y. et al. 2015. The genome of Aiptasia, a sea anemone model for coral symbiosis. Proc. Natl. Acad. Sci. USA 112:11893–8.

Baums, I. B. 2008. A restoration genetics guide for coral reef conservation. Mol. Ecol. 17:2796–811.

Bayer, T., Aranda, M., Sunagawa, S., Yum, L. K., Desalvo, M. K., Lindquist, E., Cofroth, M. A., Voolstra, C. R. & Medina, M. 2012. Symbiodinium transcriptomes: genome insights into the dinoflagellate symbionts of reef-building corals. PLoS ONE 7:e35269.

Beedessee, G., Kubota, T., Arimoto, A., Nishitsuji, K., Waller, R. F., Hisata, K., Yamasaki, S., Satoh, N., Kobayashi, J. & Shoguchi, E. 2020. Integrated omics unveil the secondary metabolic landscape of a basal dinoflagellate. BMC Biol. 18:139.

Bejerano, G., Pheasant, M., Makunin, I., Stephen, S., Kent, W. J., Mattick, J. S. & Haussler, D. 2004. Ultraconserved elements in the human genome. Science 304:1321–5.

Bellantuono, A. J., Dougan, K. E., Granados-Cifuentes, C. & Rodriguez-Lanetty, M. 2019. Free-living and symbiotic lifestyle of a thermotolerant coral endosymbiont display profoundly distinct transcriptomes under both stable and heat stress conditions. Mol. Ecol. 28:5265–81.

Berkelmans, R. & van Oppen, M. J. H. 2006. The role of zooxanthellae in the thermal tolerance of corals: a “nugget of hope” for coral reefs in an era of climate change. Proc. R. Soc. B 273:2905–12.

Bhattacharya, D., Agrawal, S., Aranda, M., Baumgarten, S., Belcaid, M., Drake, J. L., Erwin, D. et al. 2016. Comparative genomics explains the evolutionary success of reef-dwelling corals. Elife 5:e13288.

Bhattacharya, D., Yoon, H. S. & Hackett, J. D. 2004. Photosynthetic eukaryotes unite: endosymbiosis connects the dots. BioEssays 26:50–69.

Brawley, S. H., Blouin, N. A., Ficko-Blean, E., Wheeler, G. L., Lohr, M., Goodson, H. V., Jenkins, J. W. et al. 2017. Insights into the red algae and eukaryotic evolution from the genome of Porphyra umbilicalis (Bangiophyceae, Rhodophyta). Proc. Natl. Acad. Sci. USA 114:E6361–70.

Brian, J. T., Davy, S. K. & Wilkinson, S. P. 2019. Multi-gene incongruence consistent with hybridisation in Cladocinium (Symbiodiniaceae), an ecologically important genus of coral reef symbionts. Peer J 7:e7178.

Brodie, J., Ball, S. G., Bouget, F.-Y., Chan, C. X., De Clerck, O., Cock, J. M., Gachon, C. et al. 2017. Biotic interactions as drivers of algal origin and evolution. New Phytol. 216:679–81.

Cardozo, K. H. M., Guaratini, T., Barros, M. P., Falcão, V. R., Tonon, A. P., Lopes, N. P., Campos, S., Torres, M. A., Souza, A. O., Colepicolo, P. & Pinto, E. 2007. Metabolites from algae with economical impact. Comp. Biochem. Physiol. C Toxicol. Pharmacol. 146:60–78.

Carlos, A. A., Baillé, B. K., Kawachi, M. & Mandarima, T. 1999. Phylogenetic position of Symbiodinium (Dinophyceae) isolates from tridacnids (Bivalvia), cardiids (Bivalvia), a sponge (Porifera), a soft coral (Anthozoa), and a free-living strain. J. Phycol. 35:1054–62.

Chen, Y., González-Pech, R. A., Stephens, T. G., Bhattacharya, D. & Chan, C. X. 2020. Evidence that inconsistent gene prediction can mislead analysis of dinoflagellate genomes. J. Phycol 56:6–10.

Coffroth, M. A. & Santos, S. R. 2005. Genetic diversity of symbiotic dinoflagellates in the genus Symbiodinium. Prog. Biogeosci. 156:19–34.

Correa, A. M. S., Welsh, R. M. & Vega Thurber, R. L. 2013. Unique nucleoencoplastic dsDNA and +ssRNA viruses are associated with the dinoflagellate endosymbionts of corals. ISME J. 7:13–27.

Cunning, R. & Baker, A. C. 2013. Excess algal symbionts increase the susceptibility of reef corals to bleaching. Nature Clim. Change 3:259–62.

Davy, S. K., Allemand, D. & Weis, V. M. 2012. Cell biology of heterotrophic dinoflagellates in the genus Symbiodinium (Dinophyceae). Annu. Rev. Mar. Sci. 4:41–63.

Dixon, G. B., Davies, S. W., Aglyamova, G. V., Meyer, E., Bay, L. K. & Matz, M. V. 2015. Genomic determinants of coral heat stress conditions. Proc. Natl. Acad. Sci. USA 112:11893–8.

Fan, X., Qiu, H., Han, W., Wang, Y., Xu, D., Zhang, X., Bhattacharya, D. & Ye, N. 2020. Phytoplankton pangeneome
reveals extensive prokaryotic horizontal gene transfer of diverse functions. Sci Adv. 6:eaax9111.
Fujise, L., Suggett, D. J., Stat, M. & Kohlke, T. 2021. Unlocking the phylogenetic diversity, primary habitats, and abundances of free-living Symbiodinaceae on a coral reef. Mol. Ecol. 30:543-60.
Garrido, A. G., Machado, L. F., Zilberberg, C. & Leite, D. C. D. A. 2020. Insights into “Symbiodinaceae phycosphere” in a coral holobiont. Symbiosis 83:23-39.
Gates, R. D., Hoegg-Guldberg, O., McFall-Ngai, M. J., Bil, K. Y. & Muscatine, L. 1995. Free amino acids exhibit anthenoxy “host factor” activity: They induce the release of photosynthetic from symbiotic dinoflagellates in vitro. Proc. Natl. Acad. Sci. USA 92:7430-4.
González-Petch, R. A., Bhattacharya, D., Ragan, M. A. & Chan, C. N. 2019. Genome evolution of coral reef symbionts as intracellular residents. Trends Ecol. Evol. 34:799-806.
González-Petch, R. A., Stephens, T. G., Chen, Y., Mohamed, A. R., Cheng, Y., Shah, S., Dougan, K. E. et al. 2021. Comparison of 15 dinoflagellate genomes reveals extensive sequence and structural divergence in family Symbiodiniaceae and genus Symbiodinium. BMC Biol. 19:73.
Gornik, S. G., Ford, K. L., Mulhern, T. D., Bacic, A., McFadden, G. I. & Waller, R. F. 2012. Loss of nucleosomal DNA condensation coincides with appearance of a novel nuclear protein in dinoflagellates. Curr. Biol. 22:2503-12.
Hackett, J. D., Yoon, H. S., Soares, M. B., Bonaldo, M. F., Casanova, T. E., Nosenko, T. & Bhattacharya, D. 2004. Migration of the plastid genome to the nucleus in the 2004. Proc. Natl. Acad. Sci. USA 101:2466-71.
Hidaka, M. 2016. Life history and stress response of scleractinian corals. In Kayanne, H. [Ed.] Coral Reef Science: Strategy for Ecosystem Synthesis and Coexistence with Humans Under Multiple States. Springer, Tokyo, Japan, pp. 1-24.
Hikosaka-Katayama, T., Koike, K., Yamashita, H., Hikosaka, A. & Koike, K. 2012. Mechanism of paternal inheritance of dinoflagellate symbionts in the acoelomorph worm Waminoa litus. Zoolog. Sci. 29:559-67.
Hirose, M., Reimer, J. D., Hidaka, M. & Suda, S. 2008. Phylogenetic analyses of potentially free-living Symbiodinium spp. isolated from coral reef sand in Okinawa. Japan. Mar. Biol. 155:105-12.
Hou, Y., Ji, N., Zhang, H., Shi, X., Han, H. & Lin, S. 2019. Genome size-dependent pca gene copy number in dinoflagellates and molecular evidence of reversion as a major evolutionary mechanism. J. Phycol. 55:37-46.
Howells, E. J., Miller, D. J., Lougheed, M. K., Le, S., Davy, S. K. & Miller, D. J. ^ 2019. Transcriptomic analyses highlight the likely metabolic consequences of colonization of a cnidarian host by non-native Symbiodiniaceae. Mol. Ecol. 30:603-11.
Lesser, M. P., Stochaj, W. R., Tapley, D. W. & Shick, J. M. 1990. Bleaching in coral reef anthozoans: effects of irradiance, ultraviolet radiation, and temperature on the activities of photosynthetic proteins. Coral Reefs 9:65-72.
Levin, R. A., Beltran, V. H., Hill, R., Kjelleberg, S., McDougald, D., Steinberg, P. D. & van Oppen, M. J. H. 2016. Sex, scavengers, and chaperones: transcriptome secrets of divergent Symbiodinium thermal tolerances. Mol. Biol. Evol. 33:3032-9.
Lesser, M. P., Stochaj, W. R., Tapley, D. W. & Shick, J. M. 1990. Bleaching in coral reef anthozoans: effects of irradiance, ultraviolet radiation, and temperature on the activities of photosynthetic enzymes against active oxygen. Coral Reefs 8:225-32.
Li, T., Yu, L., Song, B., Song, Y., Li, L., Lin, X. & Lin, S. 2020. Genome improvement and core gene set refinement of Acropora millepora clade D. BMC Biol. 12:217.
Lajeunesse, T. C., Smith, R. T., Finney, J. & Oxenford, H. 2009. Recent progress in two co-occurring types of Symbiodinium: An exploration into the genetic basis of thermal tolerance in Symbiodinium clade D. BMC Biol. 12:217.
Leggat, W., Hoegg-Guldberg, O., Dove, S. & Yellowlees, D. 2007. Systematic survey of Symbiodinium diversity and the antiquity and diversity of coral endosymbioses. Curr. Biol. 17:2570-80.
Lajeunesse, T. C., Smith, R. T., Finn, J. & Oxenford, H. 2009. Outbreak and persistence of opportunistic symbiotic dinoflagellates during the 2005 Caribbean mass coral “bleaching” event. Proc. Biol. Sci. 276:1139-48.
Lajeunesse, T. C., Wiedenmann, J., Casado-Amezúa, P., D’Ambra, L., Turnham, K. E., Nitschke, M. R., Oakley, C. A. et al. 2021. Revival of Phyllorella Geddes for host-specialized dinoflagellates, “zoxxanthellae”, in animals from coastal temperate zones of northern and southern hemispheres. Eur. J. Phycol. https://doi.org/10.1080/09670262.2021.1914863
Lang, A. S., Zhaxybayeva, O. & Beatty, J. T. 2012. Gene transfer agents: Symbiotic signaling and bacterial uptake of DNA. Nat. Rev. Microbiol. 10:472-82.
Laurion, I., Blouin, F. & Roy, S. 2004. Packaging of mycosporine-like amino acids in dinoflagellates. Mar. Ecol. Prog. Ser. 279:297-303.
Leggat, W., Hoegg-Guldberg, O., Dove, S. & Yellowlees, D. 2007. Analysis of an EST library from the dinoflagellate (Symbiodinium sp.) symbiont of reef-building corals. J. Phycol. 43:1010-21.
Leggat, W., Yellowlees, D. & Medina, M. 2011. Recent progress in Symbiodinium transcriptomics. J. Exp. Mar. Bio. Ecol. 408:120-5.
Lesser, M. P., Stat, M. & Gates, R. D. 2013. The endosymbiotic dinoflagellates (Symbiodinium sp.) of corals are parasites and mutualists. Coral Reefs 32:603-11.
Lesser, M. P., Stochaj, W. R., Tapley, D. W. & Shick, J. M. 1990. Bleaching in coral reef anthozoans: effects of irradiance, ultraviolet radiation, and temperature on the activities of photosynthetic enzymes against active oxygen. Coral Reefs 8:225-32.
Levin, R. A., Beltran, V. H., Hill, R., Kjelleberg, S., McDougald, D., Steinberg, P. D. & van Oppen, M. J. H. 2016. Sex, scavengers, and chaperones: transcriptome secrets of divergent Symbiodinium thermal tolerances. Mol. Biol. Evol. 33:3032.
Li, T., Yu, L., Song, B., Song, Y., Li, L., Lin, X. & Lin, S. 2020. Genome improvement and core gene set refinement of Acropora millepora clade D. BMC Biol. 12:217.
Shinzato, C., Mungpakdee, S., Satoh, N. & Shoguchi, E. 2014a. A genomic approach to coral-dinoflagellate symbiosis: studies of Acropora digitifera and Symbiodinium minutum. Front. Microbiol. 5:336.

Shinzato, C., Shoguchi, E., Kawashima, T., Hamada, M., Hisata, K., Tanaka, M., Fujie, M. et al. 2011. Using the Acropora digitifera genome to understand coral responses to environmental change. Nature 476:390–3.

Shinzato, C., Yasuoka, Y., Mungpakdee, S., Arakaki, N., Fujie, M., Nakajima, Y. & Satoh, N. 2014b. Development of novel, cross-species microsatellite markers for Acropora corals using next-generation sequencing technology. Front. Mar. Sci. 1:11.

Shoguchi, E., Beedessee, G., Tada, I., Hisata, K., Kawashima, T., Takeuchi, T., Arakaki, N. et al. 2018. Two divergent Symbiodinium genomes reveal conservation of a gene cluster for sunscreen biosynthesis and recently lost genes. BMC Genom. 19:458.

Shoguchi, E., Beedessee, G., Hisata, K., Tada, I., Narisoko, H., Satoh, N., Kawachi, M. & Shinzato, C. 2021. A new dinoflagellate genome illuminates a conserved gene cluster involved in sunscreen biosynthesis. Genome Biol. Evol. 13:evea2935.

Shoguchi, E., Shinzato, C., Kawashima, T., Gyoja, F., Mungpakdee, S., Kovanagi, R., Takeuchi, T. et al. 2013. Draft assembly of the Symbiodinium minutum nuclear genome reveals dinoflagellate gene structure. Curr. Biol. 23:1399–408.

Silva Lima, A. W., Leomil, L., Oliveira, I., Varasteh, T., Thompson, J. R., Medina, M., Thompson, C. C. & Thompson, F. L. 2020. Insights on the genetic repertoire of the coral Mussismilia braziliensis endosymbiont Symbiodinium. Symbiosis 80:183–93.

Singh, S. P., Klish, M., Sinha, R. P. & Håder, D. P. 2010. Genome mining of mycosporine-like amino acid (MAA) synthesizing and non-synthesizing cyanobacteria: a bioinformatics study. Genomics 95:120–8.

Singh, S. P., Kumbhar, S., Rastogi, R. P., Singh, K. L. & Sinha, R. P. 2008. Mycosporine-like amino acids (MAAs): Chemical structure, biosynthesis and significance as UV-absorbing/screening compounds. Indian J. Exp. Biol. 46:7–17.

Smith, D. J., Suggett, D. J. & Baker, N. R. 2005. Is photoinhibition of the de novo synthesis of mycosporine-like amino acids (MAAs) a determinant of coral bleaching? Proc. Natl. Acad. Sci. USA 102:125–30.

Smith, E. G., D’Angelo, C., Salih, A. & Wiedenmann, J. 2013. Screening by coral green fluorescent protein (GFP)-like chromoproteins supports a role in photoprotection of zooxanthellae. Coral Reefs 32:463–74.

Song, B. O., Morse, D., Song, Y., Fu, Y., Lin, X., Wang, W., Cheng, S., Chen, W., Liu, X. & Lin, S. 2017. Comparative genomics reveals two major bouts of gene recombination coinciding with crucial periods of Symbiodinium evolution. Genome Biol. Evol. 9:2037–47.

Soucy, S. M., Huang, J. & Gogarten, J. P. 2015. Horizontal gene transfer: building the web of life. Nat. Rev. Genet. 16:472–82.

Stat, M. & Gates, R. D. 2010. Clade D Symbiodinium in scleractinian corals: a “nugget” of hope, a selfish opportunist, an ominous sign, or all of the above? J. Mar. Biol. 2011:790715.

Stephens, T. G., Gonzalez-Pech, R. A., Cheng, Y., Mamedov, A. R., Burt, D. W., Bhattacharya, D., Ragan, M. A. & Chan, C. X. 2020. Genomes of the dinoflagellate Polarella glacialis encode tandemly repeated single-exon genes with adaptive functions. BMC Biol. 18:56.

Swain, T. D., Chandler, J. & Backman, V. 2017. Consensus thermostolerance ranking for 110 Symbiodinium phytoplasts: an exemplar utilization of a novel iterative partial-rank aggregation tool with broad application potential. Funct. Ecol. 31:172–83.

Takahashi, S., Whitney, S., Itoh, S., Maruyama, T. & Badger, M. 2008. Heat stress causes inhibition of the de novo synthesis of antenna proteins and photobleaching in cultured Symbiodinium. Proc. Natl. Acad. Sci. USA 105:4203–8.

Thomas, C. M. & Nielsen, K. M. 2005. Mechanisms of, and barriers to, horizontal gene transfer between bacteria. Nat. Rev. Microbiol. 3:711–21.

Tsujino, I. 1961. Studies on the compounds specific for each group of marine algae, I: presence of characteristic ultraviolet absorbing material in Rhodophyceae. Bull. Fac. Fish. Hokkaido Univ. 12:49–58.

Van Etten, J. & Bhattacharya, D. 2020. Horizontal gene transfer in eukaryotes: not if, but how much? Trends Genet. 36:915–25.

Waller, R. F., Slamovits, C. H. & Keeling, P. J. 2006. Lateral gene transfer of a multigene region from cyanobacteria to dinoflagellates resulting in a novel plastid-targeted fusion protein. Mol. Biol. Evol. 23:437–43.

Warner, M. E., Fitt, W. K. & Schmidt, G. W. 1999. Damage to photosystem II in symbiotic dinoflagellates: a determinant of coral bleaching. Proc. Natl. Acad. Sci. USA 96:8007–12.

Weber, M. X. & Medina, M. 2012. The role of microalgal symbionts (Symbiodinium) in holobiont physiology. In Piganeau, G. [Ed.] Genetic Insights into the Biology of Algae. Elsevier, Amsterdam, pp. 119–40.

Weis, V. M. 2019. Cell biology of coral symbioses: foundational study can inform solutions to the coral reef crisis. Integr. Comp. Biol. 59:845–55.

West, J. M. & Salm, R. V. 2003. Resistance and resilience to coral bleaching: implications for coral reef conservation and management. Gessner. Biol. 17:956–67.

Williams, A., Chiles, E. N., Conetta, D., Pathmanathan, J. S., Cleves, P. A., Putnam, H. M., Su, X. & Bhattacharya, D. 2021. Metabolomic shifts associated with heat stress in coral holobionts. Sci. Adv. 7:eabd4210.

Wittenberg, J. B. 1960. The source of carbon monoxide in the float of the Portuguese man-of-war, Physalia physalia L. Exp. Biol. 37:698–705.

Wong, J. T. Y. 2019. Architectural organization of dinoflagellate liquid crystalline chromosomes. Microorganisms 7:27.

Yamashita, H. & Koike, K. 2013. Genetic identity of free-living Symbiodinium obtained over a broad latitudinal range in the Japanese coast: phylogeny of free-living Symbiodinium. Physiological Res. 61:68–80.

Yang, F., Li, L. & Lin, S. 2020. Methylation pattern and expression dynamics of methylase and photosystem genes under varying light intensities in Fugacium kawaguiti (Symbiodiniaceae). J. Phycol. 56:1378–43.

Yoshioka, Y., Yamashita, H., Suzuki, G., Zayasu, Y., Tada, I., Kanda, M., Satoh, N., Shoguchi, E. & Shinzato, C. 2021. Whole-genome transcriptome analyses of native symbionts reveal host coral genomic novelties for establishing coral-algae symbioses. Genome Biol. Evol. 13:evea240.

Yu, L., Li, T., Li, L., Lin, X., Li, H., Liu, C., Guo, C. & Lin, S. 2020. SAGER: a database of Symbiodiniaceae and algal genomic resource. Database 2020:bzaa051.

Yuyama, I., Ugawa, N. & Hashimoto, T. 2021. Transcriptome analysis of Durusdinium associated with the transition from free-living to symbiotic. Microorganisms 9:1560.

Zayasu, Y., Satoh, N. & Shinzato, C. 2018. Genetic diversity of farmed and wild populations of the reef-building coral, Acropora tenuis. Restor. Ecol. 26:1195–202.

Zhang, H., Hou, Y., Miranda, L., Campbell, D. A., Sturm, N. R., Gaasterland, T. & Lin, S. 2007. Spliced leader RNA transsplicing in dinoflagellates. Proc. Natl. Acad. Sci. USA 104:618–23.

Ziegler, M., Arif, C., Burt, J. A., Dobretsov, S., Roder, C., Lajeunesse, T. C. & Voolstra, C. R. 2017. Biogeography and molecular diversity of coral symbionts in the genus Symbiodinium around the Arabian Peninsula. J. Biogeogr. 44:674–86.