Chapter 7
How Does the Coral Microbiome Cause, Respond to, or Modulate the Bleaching Process?

K. M. Morrow, E. Muller, and M. P. Lesser

7.1 Introduction

Coral holobionts are formed by a dynamic multipartite symbiosis with intracellular photoautotrophs in the genus *Symbiodinium*, as well as a consortium of microorganisms that include bacteria, archaea, viruses, fungi, and protists. The coral holobiont functions as a unit to provide flexible stability in the face of constant environmental stressors. Coral bleaching, or the loss of *Symbiodinium* and their pigments, has caused significant global declines in the percentage cover of reef-building corals, particularly in recent decades as global sea surface temperatures continue to rise (Lesser 2004; Hoegh-Guldberg et al. 2007). Bleaching can be caused by a number of environmental stressors including extreme fluctuations in seawater temperature (increase or decrease), high solar irradiance, sedimentation, pollution, herbicides, and reduced salinity. Hyperoxic conditions have been shown to act synergistically with solar radiation and thermal stress to produce significantly greater fluxes of reactive oxygen species (ROS) in both host tissues and *Symbiodinium* spp. that leads to photosynthetic dysfunction, apoptosis, and bleaching (Lesser 2006, 2011; Oakley et al. 2017). We now understand that different phylotypes of *Symbiodinium* sp. within each clade represent multiple phenotypes and potentially species (Thornhill et al. 2014), and display variable rates of photosynthesis, capacity

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to photoacclimate, stress tolerance, ROS production, superoxide dismutase (SOD) activity, and metabolic interchange with their hosts (Banaszak et al. 2006; Robison and Warner 2006; Reynolds et al. 2008; Suggett et al. 2008; Hennige et al. 2009; Brading et al. 2011; Lesser 2011; Buxton et al. 2012; McGinty et al. 2012; Parkinson and Baums 2014; Roberty et al. 2014; Krueger et al. 2015; Warner and Suggett 2016; Grégoire et al. 2017).

However, much less attention has been paid to the coral microbiome, which includes the *Symbiodinium*, prokaryotes and viruses, and their role in coral bleaching and the bleaching response. Microbes can exhibit extensive diversity and abilities to respond to and withstand environmental pressures, and, as with other multipartite mutualisms (Hussa and Goodrich-Blair 2013), corals may be able to take advantage of these microbial partnerships by recruiting taxa with distinct environmental tolerances that provide a means to adapt and/or acclimate to environmental change. Here, we provide some context for the importance of the coral microbiome to holobiont function. We survey what is currently known about the relationship among *Symbiodinium*, temperature stress, and the associated prokaryotes and viruses. We also examine the impact of the coral bleaching response and environmental stressors conducive to bleaching (e.g., temperature and irradiance) on coral-associated microorganisms with particular emphasis on diazotrophic (nitrogen-fixing) bacteria. In conclusion, we summarize how a shifting and potentially dysbiotic microbiome may impact the coral host in the context of bleaching.

7.2 The Coral Holobiont

Coral-associated microorganisms form an intimate and often species-specific relationship with their hosts, aiding in a number of beneficial functions (reviewed in Bourne et al. 2016) and potentially provide assisted acclimatization in the face of a changing climate (Webster and Reusch 2017). Recent reviews have proposed the term “Beneficial Microorganisms for Corals” (BMC), which defines core microbiota or microbial consortia that maintain coral health and resilience and potentially act as bioindicators of environmental stress (Peixoto et al. 2017). Coral-associated microorganisms are known to provide pathogen resistance through the production of antimicrobial compounds (Ritchie 2006; Rypien et al. 2010), catabolism of dimethylsulfoniopropionate (DMSP), and the production of sulfur-based antimicrobial compounds and antioxidants (e.g., Raina et al. 2010, 2013; Todd et al. 2010; Howard et al. 2011), as well as the acquisition and cycling of critical nutrients (i.e., carbon, nitrogen, phosphorus, metals, vitamins; Wegley et al. 2007; Raina et al. 2009; Zhang et al. 2015; reviewed in Bourne et al. 2016). Microorganisms also appear to have evolved with corals at every life history stage (Apprill et al. 2009; Sharp et al. 2012) and may be critical to their early settlement success and metamorphosis onto reef substratum (Negri et al. 2001; Webster et al. 2004; Sneed et al. 2014; Sharp et al. 2015).

Although the coral microbiome is generally found to be diverse and species specific (Rohwer et al. 2002), recent literature has demonstrated its flexibility as a result of host physiology and morphology (Thompson et al. 2015), life history stage (Sharp et al. 2012), and microhabitat within the coral substructure (i.e., mucus, tissues, gastric cavity, skeleton; Sweet et al. 2011; Ainsworth et al. 2015). The composition of the coral microbiome also varies with season, geography, and environmental influences (e.g., temperature, pollution, macroalgae; Hong et al. 2009; Littman et al. 2009; Zhang et al. 2015; Glasl et al. 2016). Thus, as with many other multipartite symbioses (reviewed in Hussa and Goodrich-Blair 2013), we are finding that the composition and function of the community are not static and appear to be influenced by host physiology, health, and the surrounding environment, likely fluctuating in time and space. There may be low- or high-abundance bacterial or archaeal phylotypes that play a core role, as well as consortia of microorganisms working together to perform critical functions, but many of the ancillary commensal microbes may simply be filling a niche or providing functional redundancy.

In comparison to the host, symbiotic microbes divide and evolve more rapidly, potentially influencing the ability of the holobiont to adapt and/or acclimate to changing environmental conditions. In this regard, van Oppen et al. (2015) hypothesized that modification of the microbiome may be one way to facilitate transgenerational acclimatization of coral reef organisms. This concept was further developed in a commentary by Damjanovic et al. (2017), in which they proposed a series of manipulative experiments to examine whether microbial mediation could aid in long-term coral stability. Subsequent perspectives have also examined the importance of microorganisms to corals as an adaptive mechanism when faced with climate change stressors such as elevated seawater temperature and $p\mathrm{CO}_2$ levels (Torda et al. 2017; Webster and Reusch 2017). By shuffling community composition of both the microbiome and *Symbiodinium* populations, in addition to acquiring new genetic material through mutation and/or horizontal gene transfer, while interacting with the surrounding seawater microbiota, the holobiont may or may not transfer advantageous microbial alterations to new generations that could help them avoid or withstand future bleaching events (Fig. 7.1; Webster and Reusch 2017). This theory also feeds into the founder effect, which occurs when a new population (e.g., coral planula microbiome) is established by a small number of individuals from a larger population (parent colony microbiome), leading to speciation and subsequent evolution in extreme cases (Barton and Charlesworth 1984). The founder effect originates in population genetics but has been applied to the study of microbiomes for some time. For example, founder populations from the human mother may be key to a more natural ecological succession of the infant gut, leading to stability within adult immune and metabolic responses (Mueller et al. 2015). In a similar manner, vertically and horizontally transmitted founder populations from acclimated coral holobionts may be key to the stability of future generations (Fig. 7.1). Although we still have much to learn about the function and flexibility of the dynamic relationship between coral host and microbiome, the theory that holobiont resilience may be positively influenced by a flexible, and potentially manipulable, multipartite symbiosis is met with hesitant optimism.

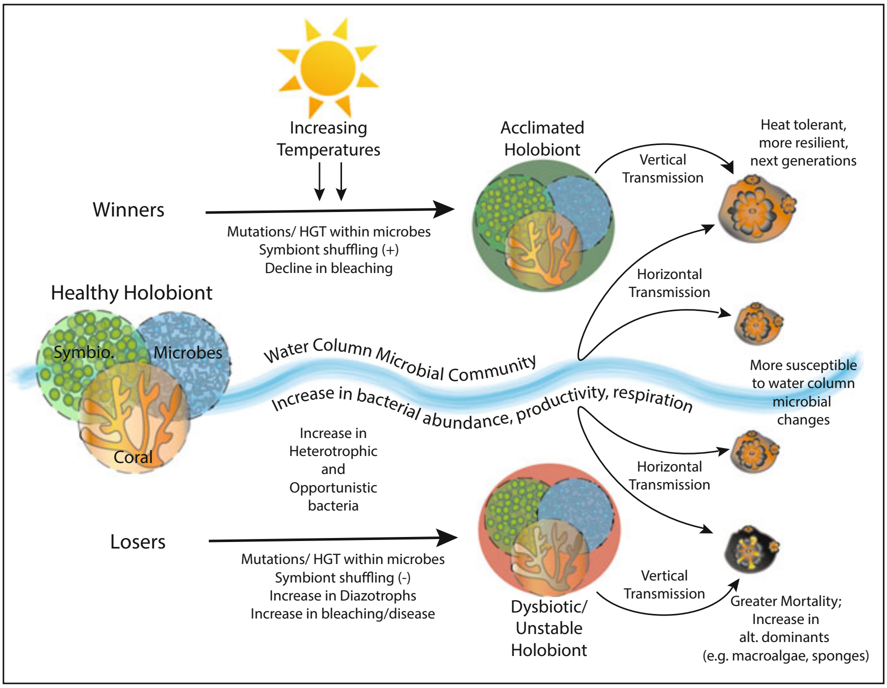

Fig. 7.1 Illustration depicts how shifts in coral microbiome and *Symbiodinium* populations, coupled with acquiring new genetic material through mutation and/or horizontal gene transfer, may be advantageous (e.g., winners) or disadvantageous (e.g., losers), to future generations of coral holobionts. Corals may be further impacted by seawater microbial community composition as this too will shift in response to changing environmental conditions and ecosystem structure resulting from repeated bleaching events [Concept adapted from Bourne et al. (2016) and Webster and Reusch (2017)]

7.3 Holobiont Response to Thermal Stress and Bleaching

For over two decades, we have known that coral bleaching events can have significant and detrimental impacts on microbial community composition (Ritchie et al. 1994), although only a handful of studies have specifically examined the impact of bleaching and the bleaching response on the coral microbiome ($n = 9$; Table 7.1). Most studies have instead focused on the impact of elevated temperature stress rather than irradiance, sedimentation, or pollution as a bleaching catalyst ($n = 15$; Table 7.1). It should be noted that although we do not include studies associated with the *Vibrio*-induced bleaching model system, we describe the concepts in Sect. 7.6.

In general, bleaching-related microbial community shifts are often characterized by a higher proportion of taxa affiliated with opportunistic bacteria (Mouchka et al. 2010), an increase in genes associated with virulence factors (Littman et al. 2011), and a shift toward *Vibrio* dominance (Bourne et al. 2008; Frydenborg et al. 2014;

Table 7.1 Summary of studies evaluating the impact of bleaching (*B*) and temperature stress (*T*) on the coral microbiome (References in chronological order)

Stressor	Impact on microbiome	Specific bacterial response	Coral spp.	Experiment type	Profiling technique	Primers	References
B	Shift in community structure	Increase in *Vibrio*/*Aeromonas* spp.	*Orbicella annularis*	In situ	Biolog plates	n/a	Ritchie et al. (1994)
B	Reduced antibacterial activity in mucus bacteria	Increase in *Vibrio* spp. dominance	*Acropora palmata*	Cultures	Assays for antibiotic activity and symbiont selection	16S (R1n/U2) BigDye direct sequencing	Ritchie (2006)
B	Shift and then recovery after stressor removed	Increase in *Vibrio* spp.	*Acropora millepora*	In situ	DGGE, clone libraries	16S DGGE (1055F/1392R) 16S clone lib. (27F/1492R)	Bourne et al. (2008)
B	Shift in bacterial community structure	Increase in *Acinetobacter* spp.	*Oculina patagonica*	In situ	Clone libraries	16S (8F/1492R)	Koren and Rosenberg (2008)
B	Shift in viral community structure	Herpes-like virus detected	*Diploria strigosa*	In situ	Metagenomics	Shotgun metagenome	Marhaver et al. (2008)
B	Healthy and bleached corals have similar dominant taxa	Higher proportion of *Vibrio* and *Acidobacteria* in bleached corals	Multiple	Both	Multiple	Multiple	Mouchka et al. (2010)
B (+4 °C)	Increase in bacteria, viruses, and shift in community structure	Increase in bacteria, viruses, and viral lytic production	*Fungia repanda*	Aquaria	Enumeration, respiration, lytic production, DGGE	16S (341F/519R)	Nguyen-Kim et al. (2015)
B	Large viral loads with VLPs found in *Symbiodinium*	Megavirus described that might infect and kill *Symbiodinium*	*Acropora aspera* and *A. millepora*	In situ	TEM and metagenomics	Nextera XT metagenome	Correa et al. (2016)

(continued)

Table 7.1 (continued)

Stressor	Impact on microbiome	Specific bacterial response	Coral spp.	Experiment type	Profiling technique	Primers	References
B	No change in overall community composition; decrease in diversity	Increase in diazotrophs	*Pocillopora verrucosa*	Aquaria	Illumina MiSeq and qPCR	nifH (F2/R6) & 16S (16SMiSeq-Andersson)	Pogoreutz et al. (2017)
T (+TOC, pH, nutrients)	Microbiome shift to more disease-associated state (i.e., virulence genes, disease-associated sequences)	Selection of virulence gene containing *Vibrio* spp.	*Porites compressa*	Aquaria	GenomiPhi amp + 454 metagenomes	n/a	Vega Thurber et al. (2009)
T (32 °C)	Bacterial shifts associated with juv. corals hosting *Symbiodinium* clade D but not clade C1	Increase in *Vibrio* spp. unless corals previously exposed to elevated temperatures in field	Juvenile *Acropora tenuis*	Aquaria	DGGE, clone libraries	16S clone lib. (63F/1387R) 16S DGGE (1055F/1392R)	Littman et al. (2010)
T	Diversity unchanged	n/a	*Acropora millepora*	Aquaria	DGGE	16S (341F/907R)	Bellantuono et al. (2011)
T (31 °C)	Antibiotic-treated corals had tissue loss	n/a	*Pocillopora damicornis*	Aquaria	Biolog EcoPlates	n/a	Gilbert et al. (2012)
T (30 °C)	Commensal bacteria suppressed by opportunistic pathogens	Increase in *Vibrio* spp. due to better substrate use	*Acropora palmate* mucus	Cultures	*chi*A qPCR, glycosidase, and protease assays	*chi*A and housekeeping genes	Frydenborg et al. (2014)
T (+2.5 and +4 °C)	Threefold increase in diazotroph diversity and richness	Increase in *Alphaproteobacteria*, including *Azospirillum*, *Rhizobium*, and *Rhodobacter*-like sequences	*Mussismilia harttii*	Aquaria	qPCR, DGGE, clone libraries	nifH clone lib. (FGPH19/PolR)	Santos et al. (2014)

T (31 °C)	Increase in microbiome diversity	Increase in *Vibrio* spp.	*Pocillopora damicornis*	Aquaria	Illumina MiSeq	16S (27F/1392R +27F/519R 16S *Vibrio* (VF169/ Vib2_R)	Tout et al. (2015)
T	Diversity unchanged in *OF* but *GV* microbiome highly variable but diversity declined	Within *GV*, shifts in *Clostridia*, *Oceanospirillales*, and *Pseudomonadaceae*	*Orbicella faveolata (OF)* *Gorgonia ventalina (GV)*	In situ	Roche 454	16S (27F/338R)	Tracy et al. (2015)
T (26–33 °C)	Bacterial community shift between coral mucus and tissues	Increase in *Alphaproteobacteria*, *Verrucomicrobiae*, *Cyanobacteria*, *Flavobacteriia*, and *Sphingobacteria*	*Acropora muricata*	Aquaria	Roche 454	16S (968F/ 1391R)	Lee et al. (2015)
T (26–31 °C)	Increase in diversity and richness; change in mucus composition	Increase in *Alphaproteobacteria* and *Verrucomicrobiae*; decrease in *Gammaproteobacteria*	*Acropora muricata*	Aquaria	Roche 454	16S (968F/ 11391R)	Lee et al. (2016)
T (+ algae, nutrients)	Algal contact + T-destabilized coral microbiome; increased variability	Increase in *Vibrionales and Oscillatoriales*; decline in *Synechococcus*	*Porites*, *Siderastrea*, and *Agaricia*	In situ	Roche 454	16S (515F/ 806R)	Zaneveld et al. (2016)
T (32 °C)	Stable first 10 days; alpha diversity decreased and richness unchanged	Decline in *Rhodobacterales*; increase in *Alteromonadales*, *Vibrionales*, and *Flavobacteriales*	*Acropora digitifera*	Aquaria	Illumina MiSeq	16S (515F/ 806R)	Gajigan et al. (2017)

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Table 7.1 (continued)

Stressor	Impact on microbiome	Specific bacterial response	Coral spp.	Experiment type	Profiling technique	Primers	References
T	Stress-induced upregulation of viruslike gene expression in *Symbiodinium*	Nucleocytoplasmic large DNA viruses found in *Symbiodinium* cultures	*Symbiodinium* cultures	Aquaria	Transcriptomics (no replication)	Whole transcriptome	Lawrence et al. (2017)
T (+4 °C)	Shifts in gene expression levels of viruses infecting heat-stressed symbiont cultures	Nucleocytoplasmic large DNA viruses and novel + ssRNAV detected	*Symbiodinium* cultures	Aquaria	Illumina HiSeq	Whole transcriptome	Levin et al. (2017)
T (29–35 °C)	Microbiome rapidly shifts (<20 h); microbiome response predicted by prior exposure to T stress	Increase in *Alphaproteobacteria* and *Cyanobacteria*	*Acropora hyacinthus*	In situ, transplant, and aquaria	Illumina MiSeq	16S (784F/1061R)	Ziegler et al. (2017)

Tout et al. 2015; Table 7.1), although some corals, such as *Porites lobata* (Hadaidi et al. 2017) and *Orbicella faveolata* (Tracy et al. 2015), are still able to maintain stable microbiomes through bleaching events. More recently, research has specifically focused on the impact of elevated temperatures on the coral microbiome, finding that even a single stressor can cause significant shifts in the microbiome, often increasing diversity (McDevitt-Irwin et al. 2017; Table 7.1), and the abundance of opportunistic bacteria such as *Vibrio* spp. (Littman et al. 2010; Frydenborg et al. 2014; Tout et al. 2015; Gajigan et al. 2017).

The coral microbiome itself may have a temperature tolerance threshold, as it was found that bacterial community changes occurred at temperature elevations >1 °C, with no evidence of community shifts at lower-temperature changes (Salerno et al. 2011). Other studies have demonstrated a link between temperature stress and bacteria associated with nitrogen cycling (reviewed in Sect. 7.3.1; Santos et al. 2014; Ziegler et al. 2017). Similar patterns emerge when corals are exposed to the compounding effects of multiple stressors (i.e., elevated temperatures, dissolved organic carbon, pH, and/or nutrients), causing shifts in the microbiome community toward a dysbiotic state, or disturbance of the "normal flora," which may be associated with a disease state leading to bleaching and/or mortality (Rosenberg et al. 2007; Vega Thurber et al. 2009; Zaneveld et al. 2016). Zaneveld et al. (2016), in a 3-year field study, showed that chronic exposure to eutrophication, algal overgrowth (e.g., simulated overfishing), and temperature stress destabilized coral microbiomes making them more susceptible to the effects of future exposures. Webster et al. (2016) also demonstrated a significant interactive effect of thermal stress and ocean acidification on the microbial communities of corals and other important calcifying species on coral reefs. These studies, and others outlined below, demonstrate that microbiomes can change rapidly in response to moderate to severe environmental stress, potentially aiding in the adaptability of their host (proposed in Webster and Reusch 2017; Peixoto et al. 2017) and/or leading to their destabilization and loss of critical functions (Zaneveld et al. 2016; McDevitt-Irwin et al. 2017; Fig. 7.1).

A recent meta-analysis found that stress, particularly during climate anomalies, is implicated in an increase in community diversity and a decline in the relative abundance of potentially key coral endosymbionts in the genus *Endozoicomonas* (class *Gammaproteobacteria*, order *Oceanospirillales*; McDevitt-Irwin et al. 2017). Members of the *Endozoicomonas* genus are often dominant members of coral microbiomes (Morrow et al. 2012; Bayer et al. 2013; Rodriguez-Lanetty et al. 2013) and can be found deep within coral tissues (Bayer et al. 2013; Neave et al. 2016a). They are hypothesized to prevent mitochondrial dysfunction and promote gluconeogenesis (Ding et al. 2016), aid in sulfur cycling (Neave et al. 2016b), and protect the coral from bleaching pathogens (Pantos et al. 2015), potentially through the production of quorum-sensing metabolites (Mohamed et al. 2008) or antimicrobial compounds (Rua et al. 2014). McDevitt-Irwin et al. (2017) and others (Zaneveld et al. 2016) provide evidence that suggests the coral microbiome becomes more diverse (increased richness), more variable (reduced evenness), and less stable when under stress. Interestingly, a similar pattern has emerged in human microbiome studies, where once it was believed that a dysbiotic state was characterized by low diversity and overabundant opportunistic or pathogenic taxa (Lozupone et al. 2012); more recent studies show that human microbiomes can also become more variable under stress (reviewed in Zaneveld et al. 2017). Perhaps this discrepancy has to do with the time frame in which we are sampling microbiomes, capturing the community as it transitions from a healthy equilibrium through a variable dysbiotic state to an alternate stable state characterized by pathogens and disease symptoms (reviewed in Bourne et al. 2016). In fact, communities are more often in a transient state of disturbance than stability, and some have suggested we shift our focus to studying alternate transient states, rather than alternate stable states, in order to make more relevant predictions about community assembly (Fukami and Nakajima 2011). Nevertheless, it would likely be difficult for the coral to return to a healthy equilibrium after a stressor is alleviated, leading to a reduction in overall ecosystem resilience, unless the ability of the coral microbiome to shift and acclimate to changing environmental conditions confers some adaptive advantage to the coral host.

One of the best examples that the coral microbiome may actually preadapt a coral to survive thermal stress is a recent study by Ziegler et al. (2017), which presents experimental data demonstrating that the microbiome of heat-sensitive and heat-tolerant corals is significantly different and that heat-tolerant corals exposed to bleaching temperatures showed no changes in their microbiomes and bleached less often. In these experiments, corals (*Acropora hyacinthus*) were exposed to both a long-term (17-month) reciprocal transplant experiment between two thermally distinct environments and a short-term heat-stress experiment. Coral microbiomes were shown to rapidly adjust to new environmental conditions (~20 h), and the thermal environment from which the corals originated (17-month experiment) predicted their microbial response to heat stress. These results suggest that long-term exposure to environmental stress such as thermal variability allows the coral microbiome to acclimatize, which in turn may play a role in a coral's resistance to thermal stress (Fig. 7.1). In an earlier laboratory-based study (Bellantuono et al. 2011), *Acropora millepora* corals were exposed to temperatures 3 °C below the bleaching threshold (generally defined as ~1 °C above summer maximum) in a short-term (10-day) experiment, which resulted in a significant reduction in bleaching susceptibility. However, no changes were detected in the *Symbiodinium* populations based on internal transcribed spacer region 2 (ITS2) sequencing or bacterial populations based on denaturing gradient gel electrophoresis (DGGE) results from a single time point 6-days into the experiment. The authors concluded that rapid temperature acclimation may be a function of host physiological plasticity rather than shifts in the symbiont community. In another study, antibiotics were applied every day over the course of a heat-stress experiment to reduce the bacterial activity associated with *Pocillopora damicornis* corals while monitoring the coral holobiont response to thermal stress (Gilbert et al. 2012). Microbial viability and activity were monitored with 96-well Biolog EcoPlates™, an assay panel that measures bacterial carbon metabolism. The heat-stressed and antibiotic-treated holobiont displayed significantly depleted host protein levels, chlorophyll *a* concentrations, and tissue loss in comparison to corals with an intact (i.e., unmanipulated) microbiome, again suggesting that the microbial consortium may provide some resilience against thermal stress. Thus, although thermal acclimatization has been widely demonstrated in reef corals (Brown et al. 2002a, b; Middlebrook et al. 2008; Barshis et al. 2010; Palumbi et al. 2014 among others), these recent studies are the first to demonstrate the potential role of the microbiome in host stability and thermal tolerance.

7.3.1 Diazotrophy and the Bleaching Response

Nitrogen is a critical and limiting nutrient that corals generally acquire through the uptake of dissolved inorganic nitrogen or heterotrophic feeding. Several studies have demonstrated the presence of nitrogen-fixing bacteria (diazotrophs) in the coral microbiome (e.g., Lesser et al. 2004) and that "new" nitrogen can be obtained from these members of the coral microbiome (Lesser et al. 2007a). More broadly, there is evidence suggesting that there is a critical link between coral bleaching and the availability of environmental nitrogen (Wooldridge 2013; Vega Thurber et al. 2014; Shantz et al. 2016; Pogoreutz et al. 2017). In fact, an increase in the acquisition of nitrogen through heterotrophy has been shown to reduce post-bleaching photoinhibition and recovery times (Grottoli et al. 2006; Ferrier-Pagès et al. 2010; Hoogenboom et al. 2012). To this end, Godinot et al. (2011) demonstrated that elevated temperatures (33 °C) caused a severe decrease in nitrate and ammonium uptake rates, even leading to release of nitrogen into seawater. Furthermore, the combination of high temperature (33 °C) and low pH (7.5) resulted in a significant decline in phosphate and nitrate uptake rates, although these would be the ecological extremes for tolerable temperatures and pH (Godinot et al. 2011).

From the perspective of diazotrophy (i.e., bacteria and archaea that fix atmospheric nitrogen gas into a more usable form such as ammonium), daylight dinitrogen (N_2) fixation was shown to significantly increase in corals exposed to a 6 °C temperature increase in comparison to controls (Cardini et al. 2016). Corals exposed to nitrogen-enriched seawater also demonstrated an increase in photoprotective pigment concentrations while maintaining rates of photosynthesis and calcifications at ca. 60% and 100% of rates for unenriched controls that experienced a significant decrease in photosynthesis and calcification (Beraud et al. 2013). The authors suggest that inorganic nitrogen availability may be akin to heterotrophic feeding in maintaining coral metabolism under stressful conditions.

Based on the above experiments, it is, therefore, not surprising that recent research has also documented an increase in the abundance and diversity of coral-associated diazotrophic bacteria during thermal stress events. Diazotroph diversity and richness within *Mussismilia harttii* corals increased by threefold during both a 2.5 and 4 °C experimental temperature increase (Santos et al. 2014). Pogoreutz et al. (2017) also documented a significant increase in diazotrophic activity during a 28-day, sugar-induced bleaching experiment with *Pocillopora verrucosa* corals. Although the Pogoreutz et al. (2017) study may not be ecologically relevant, they demonstrated the impact of bleaching on the diazotrophic community without the confounding effects of heat and light stress. High temperature and light also increase rates of organic matter release by corals into seawater which could further enhance pelagic N_2 fixation rates (Böttjer et al. 2016). Ainsworth et al. (2015) identified two potential N_2-fixing bacteria as intracellular within *Symbiodinium* and within *Symbiodinium*-containing coral cells (*Actinomycetales* and *Ralstonia*, respectively), using fluorescent in situ hybridization (FISH) and 16S rRNA gene-targeted sequencing (454 tag sequencing). Both identified phylotypes can also form diazotrophic symbiotic associations in other photosynthetic systems (Chen et al. 2003; Sellstedt and Richau 2013). Finally, although diazotrophs were not specifically examined, Ziegler et al. (2017) identified bacteria affiliated with the class *Alphaproteobacteria* (e.g., *Rhodospirillaceae*, *Rhizobia*) as responsible for a large fraction of the functional enrichment within heat-tolerant corals, as opposed to *Gammaproteobacteria* (e.g., *Hahellaceae*, *Alteromonadaceae*, *Vibrionaceae*), within heat-sensitive corals. Similarly, Lee et al. (2016) documented an increase in *Alphaproteobacteria*, *Verrucomicrobiae*, and *Cyanobacteria* in the mucus of thermally stressed corals preceding a bleaching event. Members of the *Alphaproteobacteria* and *Cyanobacteria* are often associated with nitrogen cycling in host-associated microbiomes (Lesser et al. 2004, 2007b; Tsoy et al. 2016).

As noted above, an increase in available nitrogen may benefit corals under thermal stress; however, too much may interfere with the internal equilibrium between host and *Symbiodinium*, potentially contributing to the bleaching response. Diazotrophy in corals has been shown to increase the *in hospite* growth rates of *Symbiodinium* under normal environmental conditions without an increase in biomass (Lesser et al. 2007a), presumably from a host-controlled increase in symbiont losses. This was hypothesized to be offset by an increase in daily turnover rates of *Symbiodinium* (Lesser et al. 2007a). Higher levels of nitrogen supplied by diazotrophic bacteria would likely release *Symbiodinium* completely from N-limited growth and cause high rates of cell division and reduced translocation of photosynthates to the coral (Falkowski et al. 1993; Dubinsky and Jokiel 1994; Suescún-Bolívar et al. 2016). Pogoreutz et al. (2017) theorize that retaining photosynthates could result in the energy limitation of coral carbon-concentrating mechanisms (CCMs), which would result in carbon (i.e., CO_2) limitation within photosynthetic dark reactions, causing a heightened susceptibility to photodamage and subsequent bleaching (i.e., sink limitation). Stimulated nitrogenase activity due to elevated temperatures leading to a further increase in coral-associated diazotrophic activity is believed to be another mechanism by which the internal nutrient equilibrium within the coral holobiont becomes imbalanced, disrupting the N-limited state of *Symbiodinium* and potentially inducing or prolonging bleaching events (Rädecker et al. 2015; Fig. 7.2). Pernice et al. (2012) clearly demonstrated the importance of ammonium (NH_4^+) uptake from the surrounding seawater, while Cardini et al. (2015) demonstrated that on a seasonal basis some corals could become more dependent on the contribution of fixed N_2 for their nitrogen budgets. These studies suggest that coral-associated nitrogen fixers may be more intimately tied with *Symbiodinium* and the coral bleaching response than we currently understand (Fig. 7.2).

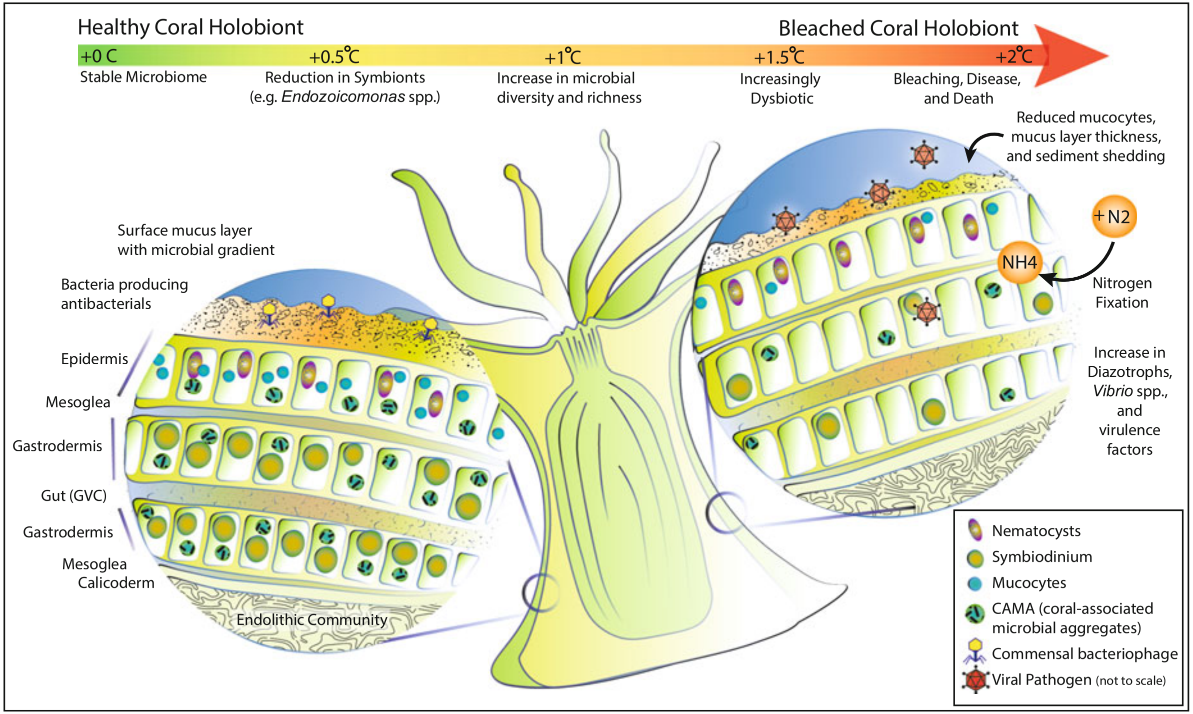

Fig. 7.2 Illustration depicts hypothesized physiological changes to the coral host and shifts in the microbial communities as a coral is exposed to increasing temperature stress. Coral mucocytes are reduced, mucus composition changes, and surface mucus layer thickness is reduced in corals experiencing bleaching temperatures, which may disrupt the microbiome composition and bacterial/viral gradient, impeding the protective benefits of high lytic activity within intermediary mucus layers. The relative abundance of putative symbionts (e.g., *Endozoicomonas* spp.), within coral-associated microbial aggregates (CAMA) decline, and bacteria affiliated with pathogens (e.g., *Vibrionales*) are stimulated. Diazotrophy (nitrogen fixation) increases as temperatures increase, which may release *Symbiodinium* from N-limited growth, causing higher rates of cell division, reduced translocation of photosynthates, and ultimately leading to greater susceptibility to photodamage and subsequent bleaching

7.3.2 Coral Mucus and the Mucus Microbiome in Response to Bleaching

Thermal stress and bleaching can also cause a compositional change in coral mucus (Wooldridge and Done 2009), which is a protective boundary layer between the coral tissues and external environment where the majority of the microbiome takes up residence, in a similar manner to the mucosal community of the human gut (Smillie et al. 2011). The surface mucus layer is loosely defined as a polysaccharide-protein-lipid complex secreted by epithelial mucocytes onto the coral surface (reviewed in Brown and Bythell 2005). Mucus production by corals not only aids in feeding and self-cleaning but also provides protection against pathogens, desiccation, UV radiation, pollutants, and other physical damage (Brown and Bythell 2005; Bythell and Wild 2011; Barr et al. 2013a). Much of the fixed carbon within the mucus layer originates from the *Symbiodinium* and serves as a rich food source for bacteria (Ritchie and Smith 2004). By providing a stable growth medium for both beneficial and detrimental bacteria, mucus plays a key role in a coral's innate immune function, enhancing susceptibility or providing protection from pathogens (Ducklow and Mitchell 1979; Banin et al. 2001; Lipp and Griffin 2004). However, as the composition of coral mucus is altered by thermal stress events, so will the stability of the mucus- and tissue-associated microbiome.

Coral bleaching and thermal stress increase organic matter and mucus production in some corals (Niggl et al. 2009) while decreasing mucus thickness in others (i.e., *Diploria* sp.; Pratte and Richardson 2014). For example, the chemical composition of *Acropora muricata* coral mucus was altered in experimentally thermally stressed corals (26–33 °C), causing a change in the proportion of simple sugars (e.g., fucose, glucose, and mannose) and a reduction in the proportion of *N*-acetyl glucosamine and C6 sugars, which also correlated with a shift in the coral-associated microbial community (Lee et al. 2016). A drop in the relative abundance of *Gammaproteobacteria* was associated with a change in the content of fucose and mannose sugars, and an increase in *Cyanobacteria* was correlated with shifts in arabinose and xylose (Lee et al. 2016). Furthermore, these changes in the composition of the mucus and microbiome began at 29 °C, prior to visual signs of bleaching, which occurred at 31 °C, suggesting that mucus composition could be used as a bioindicator of pre-bleaching conditions.

In a seminal paper describing the coral mucus microbiome, Ritchie (2006) demonstrated that healthy *Acropora palmata* mucus selected for bacteria that produced antibiotics active against a putative coral pathogen (*Serratia marcescens* PDL100). Not only was antibiotic activity lost during a summer bleaching event (i.e., increased temperatures), but coral tissues were dominated by bacteria affiliated with the genus *Vibrio*. Since then, several studies have also shown a reduction in antibacterial activity of mucus-associated bacteria under elevated temperature stress (Shnit-Orland and Kushmaro 2009; Rypien et al. 2010). Recent work has suggested additional mechanisms for the suppression of opportunistic pathogens by coral-associated commensal bacteria. For example, Frydenborg et al. (2014) demonstrated that *Vibrio* spp. were better able to use key substrates found in coral mucus (e.g., α-D-glucopyranosidase), allowing them to outcompete commensal coral bacteria under elevated temperatures. Lee et al. (2015) also demonstrated that the relative abundance of *Vibrio* spp. increased and the putative symbiont, *Endozoicomonas* spp., decreased at pre-bleaching temperatures (29 °C). Interestingly, this declining trend continued for *Endozoicomonas* spp., but the abundance of *Vibrio*-related OTUs also declined in the tissues but increased in the mucus layer as the coral reached bleaching temperatures (31 °C; Lee et al. 2015), perhaps avoiding the toxic environment developing within the coral tissues.

Thermally bleached corals have also demonstrated a reduced capacity to remove sediments (Bessell-Browne et al. 2017), which are laden with bacteria and viruses (Breitbart et al. 2004). Sedimentation and water turbidity can result from both anthropogenic activities (e.g., dredging, coastal runoff) and weather events. The removal of sediments is not only energetically costly (Peters and Pilson 1985; Riegl and Branch 1995) but has also been associated with the transmission of pathogens (Hodgson 1990) and increased disease prevalence (Haapkylä et al. 2011; Pollock et al. 2016). Bleaching may further interfere with sediment removal by reducing the number of epithelial mucocytes (Fitt et al. 2009; Piggot et al. 2009), as well as reduced mucus within the deeper gastrodermal layers (Fitt et al. 2009). Increased accumulation of sediments on bleached corals can lead to mucus sheet formation (Bessell-Browne et al. 2017), necrosis (Weber et al. 2012), and ultimately mortality. These studies indicate that the structure and composition of coral mucus can change under thermal stress and bleaching events (see also Krediet et al. 2009; Mao-Jones et al. 2010), which may lead to an environment that is less stable and more attractive to opportunistic microorganisms and pathogens than beneficial symbionts (Fig. 7.2).

Bacteriophages (i.e., a virus that infects and replicates within a bacterium) also play a dynamic and little recognized role in the development and maintenance of coral mucosal communities and have been shown to shift their community composition during environmental changes, including disease states (Columpsi et al. 2016; Soffer et al. 2015). Bacteriophage adherence to mucus (BAM) describes how phage can directly attach and interact with coral mucins (Barr et al. 2013a), displaying specific bacterial hunting behavior and potentially aiding in phage-mediated immunity (Barr et al. 2013b). The coral mucus layer is thought to be spatially structured in a similar manner to other metazoans (Johansson et al. 2011), forming a gradient from the seawater interface where microbial abundance is highest to the coral epithelium where microbial abundance is lowest and mucin production is greatest (Fig. 7.2). Silveira and Rohwer (2016) proposed that this gradient supports greater viral lysogeny at the mucosal-seawater interface, protecting coral commensals from superinfection and increasing their fitness, while deeper layers are protected from invading pathogens via higher levels of phage infection and cell lysis. High lytic activity within the intermediary mucus layers likely facilitates diversification of the bacterial community, aiding in the maintenance and assembly of a healthy microbial community by providing spatial refuges and coexistence stabilization (Schrag and Mittler 1996; Klimenko et al. 2016). Therefore, shifts in the structure and thickness of mucus resulting from environmental stress or disease may increase the proximity of microbes to the coral epithelium (Earle et al. 2015), shifting the phage-mediated immunity mechanisms and potentially allowing for invasion by lysogenic pathogens leading to the onset of infection (Fig. 7.2).

7.4 Microbiome-*Symbiodinium* Interactions

The control of the composition of the coral microbiome may be dependent on multiple factors, including host age, genotype and clade, *Symbiodinium* phylotype, and/or the environment (Hernandez-Agreda et al. 2016). In particular, the presence of photosymbionts is believed to influence the composition of host microbiomes through the release of a complex array of organic exudates (e.g., DMSP, amino acids, and polysaccharides; Bourne et al. 2013). Habitat-specific environmental differences have also been shown to drive the composition of the microbiome in sponges (Morrow et al. 2016) and in corals (Pantos et al. 2015). This may be why Hernandez-Agreda et al. (2016) identified a distinct group of bacteria associated with one coral species across multiple habitat types. Other studies have identified additional features of the host that are deterministic for the community structure of the coral microbiome (Williams et al. 2015; Apprill et al. 2016).

The growth and density of *in hospite Symbiodinium* populations are highly dependent on nitrogen availability; therefore, microorganisms that mediate nitrogen cycling within the holobiont may have consequences for the stability of these critical dinoflagellate populations (see Sect. 7.3.1). For example, diazotrophs (N_2-fixing bacteria and archaea) have been estimated to provide as much as 11% of the *Symbiodinium* nitrogen requirements (Cardini et al. 2015). Recent research has also confirmed earlier observations (Lesser et al. 2007a) that the majority of fixed nitrogen is translocated to the *Symbiodinium* compartment and is largely driven by bacteria affiliated with the *Alpha*- and *Gammaproteobacteria*, including the orders *Rhizobiales* and *Rhodobacterales* (Olson and Lesser 2013; Lesser et al. 2017). Members of the *Cyanobacteria* (Lesser et al. 2007a), fungi (Wegley et al. 2007), and archaea (Siboni et al. 2012) are also implicated in nitrogen cycling within corals. Also, common diazotrophs such as *Rhizobia* are found in early life stages, suggesting that these relationships develop early and provide critical photosymbiont stability within the holobiont (Lema et al. 2014).

Additional interactions between *Symbiodinium* and bacteria have been identified; for example, bacteria affiliated with the order *Roseobacterales* (within the class *Alphaproteobacteria*) were shown to form obligate associations with *Symbiodinium* in laboratory cultures and may increase *Symbiodinium* growth rates (Ritchie 2012). The *Roseobacterales*, along with other coral-associated bacteria (e.g., *Endozoicomonas*, *Halomonas*), are also affiliated with sulfur cycling in the coral holobiont (Raina et al. 2009; Todd et al. 2010). Sulfur compounds such as dimethylsulfoniopropionate (i.e., DMSP) and its breakdown products can act as antioxidants that may protect *Symbiodinium* from photosynthesis-derived oxidative stress (Sunda et al. 2002; Deschaseaux et al. 2014). Furthermore, a strong negative correlation has been demonstrated between the abundance of bacterial pathogens and the abundance of the proposed symbiont *Endozoicomonas* in bleaching corals (Pantos et al. 2015). This protective benefit was further alluded to in a study by Meyer et al. (2014), in which disease lesions on the coral *Porites astreoides* correlated with a low relative abundance of bacteria affiliated with *Endozoicomonas* spp. rather than with a specific pathogen. Although multiple studies indicate destabilization of the bacterial community is associated with stress (Vega Thurber et al. 2009), pathogen exposure (Welsh et al. 2017), or disease symptoms (Sunagawa et al. 2009), ultimately it is difficult to separate correlation from causation to determine whether *Endozoicomonas* spp. are responsible for protecting the coral from pathogens (Glasl et al. 2016) or are simply declining in response to stress and/or disease (Morrow et al. 2015, 2017).

It is clear that very little is known about the specific interactions between the microeukaryote *Symbiodinium* and prokaryotic components of the coral microbiome. The emerging story of the coral microbiome was preceded by theory and technical approaches pioneered by studies on the human microbiome. Similarly, the oceanographic community has been intensely interested in metabolic exchanges between phytoplankton, including dinoflagellates, and bacterioplankton in what has been called the "phycosphere" (Tang et al. 2010; Hu et al. 2015; Bolch et al. 2017). These studies have demonstrated that unique metabolic interdependencies exist within many pelagic eukaryotic-prokaryotic associations that could act as model systems to guide studies on similar interactions in symbiotic systems such as corals. One of the most well-studied examples is the *Roseobacter*-algae interaction, whereby *Roseobacter* bacteria supply vitamins, phytohormones, and antibacterial compounds to the alga (Sharifah and Eguchi 2011). However, when algal populations decline and release cell wall degradation products (i.e., *p*-coumaric acid), the *Roseobacter* shift from mutualistic partner to opportunistic pathogen, releasing 11 types of troponoids that eventually kill the alga and switch the *Roseobacter* from a sessile lifestyle to a motile, free-living cell (Sule and Belas 2013; reviewed in Ramanan et al. 2016). Thus, there is certainly potential for bacteria to play a critical role in the growth, stability, and perhaps demise of the coral-*Symbiodinium* relationship as was previously suggested in the "bacteria-induced bleaching" hypothesis (see Sect. 7.6).

7.5 Coral Bleaching in Relation to Coral Disease

While overfishing, pollution, and coastal development have long been drivers of coral reef degradation, the dominant cause of reef decline is climate change, which primarily manifests itself as coral bleaching. However, diseases with etiological agents, either primary or secondary in nature, are largely responsible for a 30% decline in worldwide coral cover over the past 30 years (Hughes et al. 2003). More recent research has predicted that coral diseases may cause as much mortality as bleaching within future decades (Maynard et al. 2015). While the assumptions of the model of Maynard et al. (2015) have been questioned (Lesser and van Woesik 2015), several other models have revealed that many coral diseases are not infectious (i.e., transmissible) and do not fit into a contagious disease model (Yee et al. 2011). Most studies are more consistent with disease prevalence being secondary to environmental stress, which leads to opportunistic coral disease outbreaks (Lesser et al. 2007b; Muller and van Woesik 2012; Randall and van Woesik 2015). A disease is defined as any impairment that interferes with or modifies the performance of normal functions, including responses to environmental factors, infectious agents, inherent or congenital defects, or combinations of these factors (Wobeser 2006). Identifying disease within corals is surprisingly difficult as there are very few macroscopic signs produced by corals to indicate poor physiological functioning. There is still little agreement on whether coral diseases are infectious or are opportunistic in nature, and many of the etiological agents still remain elusive (Lesser et al. 2007b; Apprill et al. 2013; Lesser and Jarett 2014).

Environmental stress causes coral bleaching (Fitt et al. 2001; Lesser 2011) and is also a prerequisite for the occurrence of many coral diseases (Burge et al. 2014). Indeed, environmental stress mediates the occurrence of coral disease by lowering host resistance, by increasing pathogen abundance and virulence, or through combinations of these responses (Bruno et al. 2007; Brandt and McManus 2009; Sokolow 2009; Reed et al. 2010; Muller and van Woesik 2014; Randall et al. 2014; Zvuloni et al. 2015). Even apparently healthy corals are often infected with microbes that may negatively impact health and host physiology (Miller et al. 2014). Despite improved efforts to identify the primary pathogens responsible for infection, most studies remain dependent on the macroscopic disease appearance for diagnosis (Ainsworth et al. 2007), with its associated limitations. Corals may show visual signs of disease such as bleached tissue, discoloration (darkening or abnormal pigmentation), abnormal growth, or tissue loss. But, the lack of baseline and basic epizootiological information has hindered our understanding of the relative importance of specific pathogens and environmental factors in the spread of disease epizootics. Interestingly, coral bleaching has also been associated with bacterial pathogens (see Sect. 7.6) and possibly viruses (Lawrence et al. 2015; Levin et al. 2017; see Sect. 7.7). Environmentally induced bleaching events can also increase the prevalence of infectious disease outbreaks on reefs through immune system suppression (Mydlarz et al. 2009), which could lead to an increase in disease susceptibility and longevity once infected. Furthermore, thermal stress conditions that often accompany coral bleaching can increase pathogen growth rates (Alker et al. 2001; Ward et al. 2007) and virulence (Ben-Haim et al. 2003; Kimes et al. 2012), changing commensal or mutualistic bacteria into pathogens.

7.5.1 Bleaching-Induced Disease

Coral bleaching events are often followed by infectious disease outbreaks (Guzman and Guevara 1998; Harvell et al. 2002; Bruno et al. 2007; Muller et al. 2008; Brandt and McManus 2009; Cróquer and Weil 2009; McClanahan et al. 2009; Miller et al. 2009), which may be due to a reduction in immune system function (e.g., Mydlarz et al. 2009). As discussed above most of the accumulating evidence supports the compromised host hypothesis, which suggests that the condition of the coral host, not necessarily the presence of a novel pathogen, is the primary reason for higher disease prevalence on many contemporary reefs (Lesser et al. 2007b; Muller and van Woesik 2014; Randall and van Woesik 2015). For example, during the 2005 coral bleaching event in the US Virgin Islands, Muller et al. (2008) showed that corals that had previously bleached also exhibited higher disease mortality than those that had not bleached. Corals that were resistant to high water temperatures were also more resistant to infectious diseases, which may have been because the immune system of temperature-tolerant corals was less impacted. Ritchie (2006) showed a significant reduction in antimicrobial properties within the mucus of bleached *Acropora palmata*, which allowed the proliferation of potential pathogens. Pinzón et al. (2015) also showed that genes that regulate the immune system within corals are downregulated up to a year after bleaching occurs. Therefore, as corals allocate resources in order to persist through a bleaching event, the immune system is suppressed and remains so for many months, likely increasing the probability of successful disease infection.

Although the host condition may play a critical role in disease dynamics, other research suggests thermal stress conditions may influence the behavior and pathogenicity of putative pathogens. Garren et al. (2014) showed that a bacterial pathogen, *Vibrio coralliilyticus*, uses chemotaxis and chemokinesis to target heat-stressed corals, using DMSP solely as a chemical cue to locate potential hosts. General behavior of coral pathogens also changes under different temperature conditions. For example, Garren et al. (2016) showed that *V. coralliilyticus* also increased chemotactic ability toward coral mucus when temperatures exceeded 23 °C, denoting an enhanced capability to track host-derived chemical cues. Further elevated temperatures (>30 °C) increased the pathogen's chemokinetic abilities, denoted by accelerated cell movement under favorable, mucus-rich, chemical conditions. Thermal stress has also been associated with an increase in virulence genes (Banin et al. 2003), lysis of coral cells (Ben-Haim et al. 2003), and infection by coral pathogens (Kushmaro et al. 1998; Ben-Haim and Rosenberg 2002). Thus, coral bleaching and the environmental parameters that are conducive to bleaching impact both host physiology and microbial community structure and function, setting the stage for subsequent and prolonged infections.

7.6 Bacteria-Induced Bleaching

Although region-wide mass coral bleaching events are most commonly attributed to unusually warm seawater temperatures, bleaching of the coral *Oculina patagonica* during the summer in the Mediterranean Sea was previously identified as the result of an infection with the bacterial pathogen *Vibrio shilonii* (previously referred to as

V. shiloi; Kushmaro et al. 1997). This particular *Vibrio* bacterium produces an extracellular superoxide dismutase (SOD) at 30 °C, but not at 16 °C, indicating a temperature-related virulence (Banin et al. 2003). The extracellular production of SOD protects the pathogen within the coral, allowing it to infect and persist within host tissue, producing an extracellular peptide toxin that inhibits algal photosynthesis ultimately leading to coral bleaching (Banin et al. 2000, 2003; Rosenberg et al. 2009). Extractions of the proline-rich toxin from *V. shilonii* also caused a reduction in the quantum yield of photosystem II (i.e., a sign of impending bleaching) of *O. patagonica* and *Acropora eurystoma*, but not several other Caribbean coral species, suggesting a regional or species-specific response to this potential phenomenon (Gil-Agudelo et al. 2017).

Although bacterial bleaching was documented a number of times prior to 2002, no additional cases of bacterial bleaching in *O. patagonica* have been found. This phenomenon led to the creation of the "probiotic hypothesis" (Reshef et al. 2006), whereby corals develop resistance to bacterial infection via an innate immune response or beneficial shift in their microbiome. Thus, the probiotic hypothesis was proposed as the mechanism of resistance to bacterial bleaching (Rosenberg et al. 2007), but this has been challenged based on the absence of bacteria-induced bleaching in *O. patagonica* after 2002 (Ainsworth et al. 2008). To date, corals have only been shown to possess a very basic innate immune system, although adaptive-like properties, reminiscent of higher organisms, have been documented in some coral species (Reed et al. 2010). For example, both soft and hard corals have shown a type of immunological memory and specificity for self-/nonself-recognition, with faster immunological responses after initial exposure (Hildemann et al. 1977; Salter-Cid and Bigger 1991; Jokiel and Bigger 1994). One study directly tested the probiotic hypothesis by treating colonies of *O. patagonica* with a broad-spectrum antibiotic and then exposing the coral to *V. shilonii* to determine whether infection and subsequent bleaching were influenced by the resident microbiome. As hypothesized, antibiotic-treated corals became sensitive to *V. shilonii* infection and bleached after 14 days, but non-treated corals remained healthy, presumably because beneficial members of the microbiome inhibited *V. shilonii* growth (Mills et al. 2013).

7.7 Virus-Induced Bleaching

Virus-like particles (VLPs) are present in all tissue layers of apparently healthy and diseased corals including the gastrodermis, mesoglea, and epidermis, as well as in the coral surface mucus layer (Patten et al. 2008; Leruste et al. 2012; Bettarel et al. 2013; Nguyen-Kim et al. 2014; Pollock et al. 2014; Wood-Charlson et al. 2015). It has been hypothesized that elevated temperatures and other stress events may trigger viral infections that contribute to coral bleaching and disease (Vega Thurber et al. 2008; Vega Thurber and Correa 2011; Wilson 2011; Lawrence et al. 2015; Levin et al. 2017). Wilson et al. (2001) documented VLPs associated with heat-stressed anemones, *Anemonia viridis*, and were the first to suggest that viruses may be involved in the cellular pathogenesis of bleaching. There is now growing evidence of specific and dynamic interactions between *Symbiodinium* cells and viruses or VLPs. For example, type C1 *Symbiodinium* cultures have been found to host multiple intracellular viral infections (Weynberg et al. 2017). In another study, *Symbiodinium* cultures exposed to UV demonstrated rapid cellular lysis, postulated to be from latent viral infections, although this response could also be a result of photochemical damage (Lawrence et al. 2015). Furthermore, all bleached corals exhibited large viral loads in a naturally occurring bleaching event, caused by low tide and heavy rainfall, with some VLPs specifically associated with the *Symbiodinium* cells (Correa et al. 2016).

Although our understanding of viruses and their role in host-associated microbial communities is currently limited, evidence is beginning to suggest that they play a significant role in bacterial bleaching events. Virulence factors located on chromosomal pathogenicity islands exist in some strains of *V. coralliilyticus*. The presence of these genetic signatures suggests that *V. coralliilyticus* virulence is driven by prophages and other horizontally acquired elements (Weynberg et al. 2015). During a bleaching event in the Caribbean, Marhaver et al. (2008) documented explicit changes in the absolute abundance and relative composition of viruses that infect the coral, *Symbiodinium*, and bacteria within partially bleached colonies of the massive coral, *Diploria strigosa*. More recent work has tested the theory that *Symbiodinium* are more susceptible to viral infections when exposed to heat stress. Lawrence et al. (2017) demonstrated upregulation of virus-like gene expression in cultured *Symbiodinium* cells following temperature stress experiments. Therefore, *Symbiodinium* cells may host latent or persistent viral infections that are induced via stress. These results were supported by analysis of host gene expression, which also showed changes consistent with viral infection after exposure to stress. Further to these experiments, transcriptomics were used to compare viral gene expression within thermosensitive and thermotolerant populations of *Symbiodinium* type C1 cells at ambient and elevated temperatures (+4 °C; Levin et al. 2017). This was the first study to indicate that the viruses infecting *Symbiodinium* may also be adversely affected by heat stress, further contributing to the endosymbiont's thermal sensitivity. If these results can be replicated in *Symbiodinium* cells *in hospite*, then we may begin to explain alternative hypotheses for the breakdown of the coral-*Symbiodinium* symbiosis that ultimately leads to bleaching.

7.8 Conclusions and Future Directions

Global climate change is currently ongoing and has already had a broad impact across every ecosystem on Earth (Scheffers et al. 2016). Global average temperatures have increased by 1 °C since preindustrial levels (Chap. 1). Thus, we are seeing the impact of temperature stress on the physiology and diversity of marine and terrestrial organisms around the world. Increasing global sea surface temperatures, specifically, are having a significant impact on both the macroscopic and microscopic composition of the coral reef benthos (Hughes et al. 2017), carving out space through bleaching and disease, whereby competitive dominants such as macroalgae and sponges, as well as opportunistic and heterotrophic microorganisms, will take over (reviewed in Rohwer and Youle 2010; Garren 2016). As the tropics continue to experience an increase in both the frequency and severity of high sea surface temperature events, research efforts aimed at understanding the impact of such events on both the seawater microbiome and coral-associated microorganisms will be critical to coral conservation efforts.

Coral bleaching correlates with a number of other triggers, but the combination of high temperatures and irradiance is thought to be primarily responsible (Lesser 2006, 2011). As discussed in this chapter, the impact of elevated temperature stress has been the subject of a number of coral microbiome studies, but the impact of irradiance (i.e., UV radiation; UV-R) independently or coupled with temperature stress has yet to be examined. UV-R has been demonstrated to suppress the immune system and immune response to pathogenic microorganisms in humans (Chapman et al. 1995; reviewed in Patra et al. 2016) and has been known for some time to trigger and/or exacerbate herpes simplex virus infections (Norval 2006). Studies conducted with seawater bacterioplankton communities also demonstrate that solar UV-R can differentially impact microbial activity, with greater sensitivity demonstrated by *Alphaproteobacteria* and greater resistance demonstrated by *Gammaproteobacteria* and *Bacteroidetes* (Alonso-Sáez et al. 2006). In one of the only studies to examine the impact of UV-R on the coral microbiome, solar radiation was shown to rapidly kill intracellular *Vibrio shiloi* and prevent bacteria-induced bleaching in the coral *Oculina patagonica* (Fine et al. 2002). These studies highlight the important role UV-R may have in structuring shallow-water microbial communities, particularly on coral reefs where solar irradiance has had an important influence on community structure over their evolutionary history (reviewed in Banaszak and Lesser 2009). However, because of the attenuation of UV-R with depth, and the differential effects of UV-B (290–320 nm) and UV-A (320–400 nm), most of the significant effects of UV-R may occur in shallow-reef environments ($<$ 30 m depth; Shick et al. 1996; Banaszak and Lesser 2009). There is, therefore, a need for comparative studies along depth gradients from 3 to 30 m as well as across the latitudinal extent of coral reefs, particularly in areas where temperature may remain elevated while irradiance is low.

A particularly interesting new area of research focuses on the extent to which the coral microbiome (prokaryotic and eukaryotic partners) can increase or decrease coral tolerance to specific environmental disturbances. This concept is based on defining the coral as a polygenomic metaorganism (i.e., hologenome) whereby the coral phenotype is a product of the transcriptomic, proteomic, and metabolic responses of all symbiotic partners (Putnam et al. 2017). Thus, a highly flexible microbiome that confers mechanisms for rapid holobiont acclimatization to environmental stressors associated with global climate change is met with hesitant optimism (van Oppen et al. 2015; Torda et al. 2017; Webster and Reusch 2017). Ideally, molecular-based omic techniques would be combined with microscopy approaches to allow for identification of fundamental symbionts within specific compartments (Sweet et al. 2011) and cellular microniches within the coral, for example, identifying whether microbial relationships exist with either coral or *Symbiodinium* cells and/or between specific bacterial strains. Mathematical models and network-based analytical approaches can also aid in identifying these specific microbial relationships (Sweet and Bulling 2017), followed by validation with molecular methods. Robust controls should be established for experimental studies examining the impact of environmental stressors on the coral hologenome, with the realization that experimental manipulation (e.g., transplantation, aquaria rearing) may have consequences for the stability of the microbiome leading to ecologically unrealistic conclusions (Morrow et al. 2017). Corals have demonstrated natural resilience in the face of extreme bleaching events, whereby some corals retain their symbionts and others recover their symbionts over time (Cunning et al. 2016; Hughes et al. 2017). Future research needs to take a *holistic* perspective, identifying the mechanisms driving resilience as a function of the coral metaorganism (Boulotte et al. 2016; Putnam et al. 2017; Torda et al. 2017).

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