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Coral Disease: Direct and Indirect Agents, Mechanisms of Disease, and Innovations for Increasing Resistance and Resilience

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Abstract

As climate change drives health declines of tropical reef species, diseases are further eroding ecosystem function and habitat resilience. Coral disease impacts many areas around the world, removing some foundation species

to recorded low levels and thwarting worldwide efforts to restore reefs. What we know about coral disease processes remains insufficient to overcome many current challenges in reef conservation, yet cumulative research and management practices are revealing new disease agents (including bacteria, viruses, and eukaryotes), genetic host disease resistance factors, and innovative methods to prevent and mitigate epizootic events (probiotics, antibiotics, and disease resistance breeding programs). The recent outbreak of stony coral tissue loss disease across the Caribbean has reenergized and mobilized the research community to think bigger and do more. This review therefore focuses largely on novel emerging insights into the causes and mechanisms of coral disease and their applications to coral restoration and conservation.

1. INTRODUCTION TO CORAL DISEASE

Stony coral tissue loss disease (SCTLD), dark spot syndrome, tissue sloughing, yellow band disease (also referred to as yellow blotch disease), coral tumors, white band disease, brown band disease, black band disease, bleaching—these are the phenotype-associated names for a few of the conditions that shallow scleractinian corals succumb to on reefs today (**Figure 1**). Most of these conditions lack a known definitive cause, but together they result in significant losses of already depleted corals in tropical locations such as the Caribbean (van Woesik & Randall 2017) as well as in higher latitudes (Page et al. 2023). Due to the dramatic declines in total live coral cover and/or

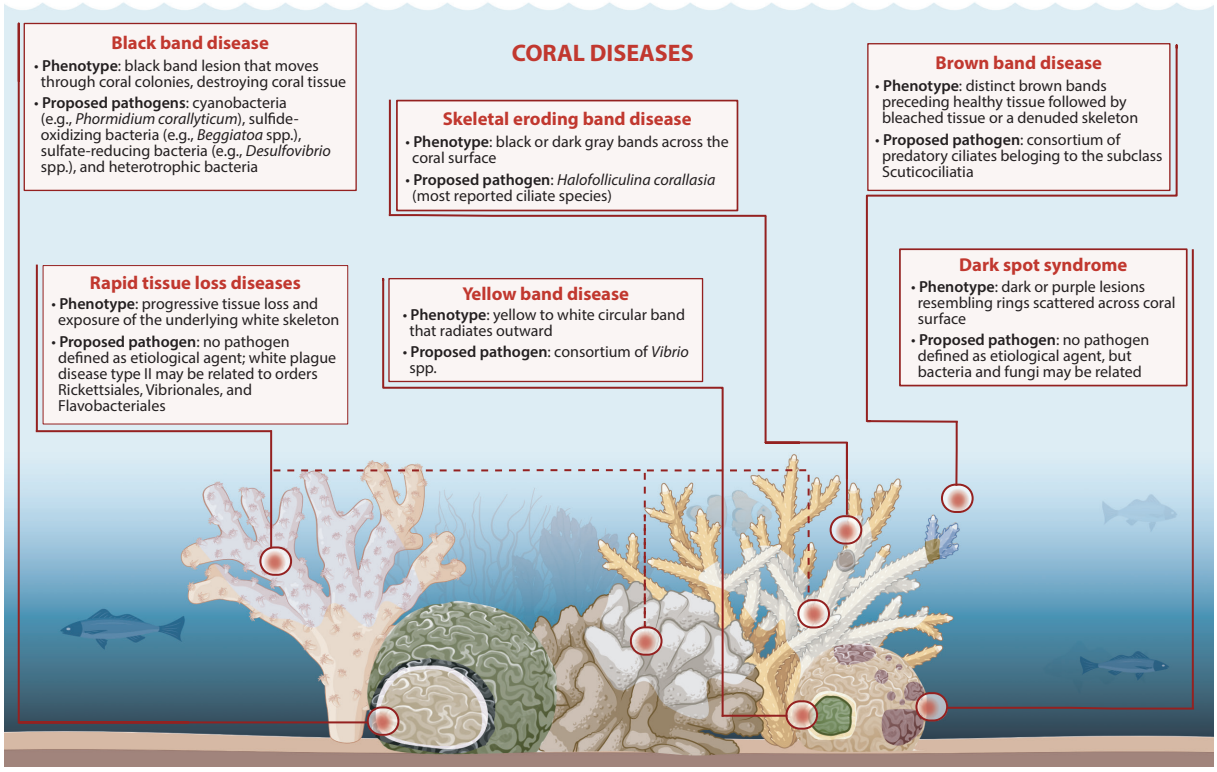

Figure 1

Named coral diseases, highlighting their visible signs and suspected pathogens.

A BRIEF HISTORY OF CORAL DISEASE RESEARCH

Coral disease research began in 1973 with the observation of black band disease reported by Antonius (Richardson 2012); a formal description was subsequently published by Rutzler et al. (1983). In 1977, the first major coral disease was described as rapid tissue loss, then termed white plague (Dustan 1977). Since then, hundreds of studies have explored coral epizootics using various methods and terms. As a result, coral disease work has had several periods driven by different but often overlapping research approaches and foci as well as changing paradigms.

From the 1970s to the 1990s, researchers focused on descriptive macroscopic signs such as changes in coloration, lack of tissue, and depression in the coral skeletons, but attempts at microscopic and culture-based methods were lacking. During this period, several disease phenotypes were described (Goreau et al. 1998), some of which were later discarded due lack of evidence to support the pathology, etiology, and epizootiology of the putative disease. Due to the novelty of the research, this foundational period was also characterized by a paucity of conceptual consensus, leading to inconsistency in our scientific nomenclature. Research in the 1990s had three areas of focus: etiological characterizations, descriptions of pathologies and host responses, and initial attempts at treatment. During this period, fulfilling Koch's postulates for putative diseases became paramount (Richardson 1998). Initial efforts to treat coral diseases with mechanical removal of pathogens, shading, and other in situ techniques were also first attempted (Griffin 1998, Hudson 2000). Despite this progress, many diagnostic data (e.g., histology and transmission electron microscopy) were inconsistently collected, limiting the comparability of the studies.

The 2000s saw major technological and theoretical advancements with the introduction of new genomic methods and the coral holobiont model (Bosch & Miller 2016, Reshef et al. 2006), allowing scientists to better investigate how corals interact with pathogens and the intersecting role of the environment and genetics in coral health. High-throughput sequencing tools (e.g., amplicons, metagenomics, and RNA sequencing) provided deeper (although often confusing) insights into mechanisms of coral diseases and coral immune responses to stress and disease. Molecular techniques also helped identify reservoirs and intermediaries involved in coral–pathogen interactions (e.g., Sweet et al. 2013b).

Across all these eras, formal incorporation of veterinary science and epidemiological modeling has advanced coral disease research. Work & Aeby (2006) unified disease naming, while researchers embraced modeling coral–pathogen interactions (Brandt & McManus 2009, Muller & van Woesik 2012). Advanced histopathology techniques helped researchers move beyond Koch's postulates by allowing them to link tissue changes to the presence or abundance of pathogens and specific processes such as tissue damage (Ainsworth et al. 2007, Gignoux-Wolfsohn & Vollmer 2015, Work & Meteyer 2014). Despite this progress, identifying a specific pathogen or even the pathogenic consortium remains challenging. In the end, for holistic coral disease research, the incorporation of a myriad of techniques, models, and theories should be attempted. We are at a point where significant advancements are being made, and working across disciplines will help crack the code of coral disease.

extirpation of coral species (Eddy et al. 2018), scientists, managers, and funding agencies have poured millions of dollars and years of human effort into trying to define the causes, conventions, and consequences of coral disease (Moriarty et al. 2020).

While coral disease research has transitioned from observational to more comprehensive approaches (see the sidebar titled A Brief History of Coral Disease Research), we still face many challenges. For example, the etiologies for the vast majority of coral diseases remain unknown. Likewise, some core epidemiological aspects of coral diseases (e.g., mechanisms of pathology, transmission, dispersion, environmental drivers, modeling, and treatments) are poorly understood. We are, however, making great strides in understanding why some corals are resistant to disease at large (MacKnight et al. 2022, Mydlarz & Muller 2023, Vollmer et al. 2023) and are testing what we can do to stop or ameliorate these outbreaks (Neely et al. 2021, Ushijima et al.

2023). Comprehensive reviews and meta-analyses have synthesized progress in understanding coral diseases over the last 20 years (Alvarez-Filip et al. 2022, Raymundo 2008, Sweet et al. 2020, Vega Thurber et al. 2020, Woodley et al. 2015), but the field continues to respond quickly to the SCTLD epizootic and the advent of new interventions. Here, we synthesize the current state of knowledge regarding scleractinian coral disease, with a strong emphasis on its interactions with restoration efforts, and make recommendations for future areas of research and innovation.

1.1. Coral Disease Descriptors and Their Etymology

There are two primary categories of coral disease: infectious and physiological. Historically, many studies have assumed that infectious agents drive most coral disease dynamics. However, many of these diseases likely fall along a spectrum, with the two categories as endpoints: Changes in host background status due to genetics and/or alterations in the environment cause shifts in coral physiology and disease susceptibility and simultaneously shift microorganisms from inconsequential to pathogenic. In this review, we focus almost exclusively on the infectious components of diseases; for more elaborate and comprehensive reviews on physiological aspects of coral disease, see the excellent works by Andersson et al. (2020), Ricci et al. (2022), Rich et al. (2021), and Spies & Takabayashi (2013).

1.2. Named Coral Diseases

According to Morais et al. (2022), 40 coral diseases have been described. Of these, 22 were detected in the Atlantic and Caribbean, and 9 were observed in the Indo-Pacific and the combined West, South, and North Pacific regions. These diseases affect approximately 200 coral species, often causing tissue loss and mass mortality (Bruckner 2015). Importantly, disease cases cannot be diagnosed by mere observation of macroscopic signs. Thus, coral disease names are not diagnostic. While environmental disturbances exceeding coral tolerance limits are known to disrupt symbiotic relationships within the coral holobiont, leaving them vulnerable, some diseases exhibit a distinct link to specific pathogens (**Figure 1**). These pathogens can be resident or transient microorganisms (Mao-Jones et al. 2010).

1.2.1. Rapid tissue loss diseases. Several widespread coral diseases share similar physiological characteristics, especially in the Indo-Pacific and Caribbean (Morais et al. 2022), making diagnosis challenging due to the lack of specific criteria for each disease (see the sidebar titled A Brief History of Coral Disease Research). Rapid tissue loss disease is therefore a collective term for diseases characterized by fast tissue loss and exposure of the underlying white skeleton. Rapid tissue losses include white band disease, white plague disease, white plague–like disease, and SCTLD.

White band disease primarily targets branching corals (Acroporidae), which are important reef builders (Aronson & Precht 2001, Ritchie & Smith 1998). The disease lesion exhibits a progressing line of tissue destruction that moves through coral colonies. This lesion starts at the base and expands progressively through branch bifurcations (Bythell et al. 2004). Turf algae often colonize exposed white skeleton after tissue loss. White band disease exhibits two forms based on the sequence of tissue death. Type I exhibits a sharp boundary between healthy tissue and exposed skeleton, resembling a plague and causing significant destruction; this type has decimated *Acropora* spp. in the Caribbean (Kline & Vollmer 2011). In contrast, type II may have a zone of bleached tissue near the disease line and can sometimes halt its progression, appearing similar to type I after stopping (Gil-Agudelo et al. 2006). Though less destructive than type I, type II's long-term impact remains concerning. While no specific pathogens have been identified for type I, researchers suggest a possible involvement of isolated bacteria or a consortium (Kline &

Vollmer 2011). For type II, potential pathogens include bacterial taxa of the orders Rickettsiales, Vibrionales, and Flavobacteriales (Gignoux-Wolfsohn & Vollmer 2015).

White plague disease is a contagious coral disease that can cause pervasive damage to reefs when widespread (Rosenberg & Loya 2004, Silva-Lima et al. 2021). It is easily recognizable by a linear white band with a diffuse border that migrates destructively through coral colonies, leaving exposed skeletons quickly colonized by algae (Bourne et al. 2015). The disease displays varying degrees of disease progression rate, classified into three types: I, II, and III. Type III is by far the most aggressive, with tissue loss rates 20 times faster than type II's (Bythell et al. 2004). The exact cause of the disease is complex and varies among coral species and locations. While the core macroscopic signs remain similar, the microbial consortium responsible differs between the Caribbean and Indo-Pacific regions. For this reason, the Indo-Pacific variant is distinguished as white plague–like disease. Several types of microorganisms, including *Vibrio* spp., *Thalassomonas* spp., cyanobacteria, and even viruses, are linked to white plague disease (Chimetto Tonon et al. 2017, Silva-Lima et al. 2021, Thompson et al. 2006).

When SCTLD was first documented in Florida, it was identified as a white plague–like syndrome because the macroscopic signs of lesion formation were similar to those previously documented for rapid tissue loss diseases within the region (Papke et al. 2024). However, the spatiotemporal ecology of this disease was so unique and tractable (during its invasion and epidemic periods) that SCTLD was soon identified as a novel coral disease; it has now spread to reefs in at least 28 countries and territories across the Caribbean, causing severe coral losses (e.g., Alvarez-Filip et al. 2022, Brandt et al. 2021, Papke et al. 2024). Often, when a reef was initially affected by SCTLD, colonies of the Meandrinidae family were the first to show signs of the disease, with rapid, persistent, and complete colony mortality followed by incidence in moderately susceptible coral species (boulder and brain corals) and then low-susceptibility species (*Porites* spp. and *Agaricia* spp.). SCTLD was also predictable spatially as it spread north and south of Miami, Florida, USA, utilizing water currents as a vector of disease spread within Florida's Coral Reef (Dobbelaere et al. 2020). It was also evident that SCTLD was likely infectious and contagious from the spatial ecology alone, and clusters could be detected across large (Muller et al. 2020) and small (Williams et al. 2021) spatial scales. Importantly, as this disease becomes endemic on a reef, differentiating the ecology of SCTLD from other endemic white plague–like mortality becomes increasingly difficult.

Dozens of studies have been published on the causes of this disease, although no single pathogen (e.g., bacterial or viral) or trigger (e.g., dinoflagellate-derived toxin) has yet been shown to be a definitive agent. Flavobacteriales are a primary suspect, but several other bacterial groups remain potential culprits (Clark et al. 2021; Heinz et al. 2024; Rosales et al. 2022, 2023). Furthermore, the utility of antibiotics in treating this disease suggests that a bacterial pathogen is involved (Ushijima et al. 2023). Viruses are also hypothesized to play a role in SCTLD etiology (see Section 2.2.3).

1.2.2. Black band disease. Black band disease is one of the most common and widespread diseases and affects several coral species around the world (Frias-Lopez et al. 2004, Richardson 1998). Its phenotype consists of a distinct black band lesion that moves across colonies, destroying coral tissue at up to several centimeters per month (Bruckner & Bruckner 2006). The band is composed of a highly structured microbial consortium dominated by the cyanobacterium *Phormidium corallyticum*, an oxygenated phototroph (Richardson & Kuta 2003); the sulfate-reducing bacteria *Desulfovibrio* spp. (Viehman et al. 2006); the sulfide-oxidizing bacteria *Beggiatoa* spp. (Richardson 1996); and other heterotrophic bacteria (Miller & Richardson 2011, Richardson 1996). This seemingly contradictory consortium creates a microcosm of contrasting environments

and is what makes black band disease so devastating (Cooney et al. 2002). While *P. corallyticum* generates oxygen at the surface, *Desulfovibrio* spp. thrive in the deeper anoxic zone, generating lethal levels of hydrogen sulfide, disrupting vital symbioses, and ultimately leading to tissue necrosis and colony death.

1.2.3. Yellow band disease. Yellow band disease was first described in Florida in 1994 (Reeves 1994), although it was likely already reported in the 1970s as "ring bleaching" by Dr. Phill Dustan. The disease manifests as a light spot surrounded by a circular yellow band at the edge (Sutherland et al. 2004). Yellow band disease targets the dinoflagellate algal endosymbionts (family Symbiodiniaceae) of corals and results in colony paling. Thus, this disease sign can easily be confused with bleaching induced by thermal stress.

Yellow band disease has different classifications and forms of occurrence according to the region where it is found. It is prevalent mainly in Caribbean reefs and affects dominant reef-building corals such as *Orbicella annularis* and *Orbicella faveolata*. Within this region, it is recognized as Caribbean yellow band disease (Randall et al. 2018, Rosenberg & Loya 2004). In the Arabian Gulf, however, this disease impacts several species from the families Acroporidae and Poritidae, manifests as a yellow band covered in mucus, and is known as Arabic yellow band disease. Within the Pacific Ocean, the disease expresses similarly to Caribbean and Arabic yellow band disease but disappears after total degradation of the tissue, as well as the loss of Symbiodiniaceae pigments (Cervino et al. 2001). Yellow band disease progresses relatively slowly (1 cm per month) and can be caused by a consortium of bacteria (*Vibrio* spp.).

1.2.4. Dark spot syndrome. Dark spot syndrome was first identified in the early 1990s in Colombia (Solano et al. 1993) and is characterized by dark lesions that resemble rings or pigmented patches scattered across coral surfaces. These circular or elongated spots, in shades of purple, black, or brown, may stem from pigment buildup within the coral symbiotic algae. While not yet classified as highly contagious or widespread, dark spot syndrome can inflict significant damage by causing tissue necrosis (Borger 2005). Its geographical range extends across both the Indo-Pacific and Atlantic Oceans, encompassing the Caribbean and reaching the Brazilian coast (Francini-Filho et al. 2008). Certain coral species, like *Stephanocoenia michelinii*, *Montastraea annularis*, and *Siderastrea siderea*, are especially susceptible (Cervino et al. 2001).

The etiology of this disease is still undefined, but bacteria and fungi are potential causes (Kellogg et al. 2014, Meyer et al. 2016, Sweet et al. 2013a). Another hypothesis suggests that it is a general stress-induced immune response (Borger 2005). Importantly, it increases in prevalence and severity during nutrient enrichment, suggesting that it is associated with reduced water quality and bleaching (Brandt & McManus 2009, Vega Thurber et al. 2014).

1.2.5. Brown band disease. First observed in the Great Barrier Reef, brown band disease poses a significant threat to scleractinian corals, particularly members of the Acroporidae, Pocilloporidae, and Faviidae (Willis et al. 2004). The disease is easily identifiable by a distinct brown band, followed by bleached tissue or a denuded skeleton. The brown band arises from a consortium of predatory ciliates belonging to the subclass Scuticociliatia. The ciliate lesion migrates from the base to the tip of branching corals (Bourne et al. 2008, Ulstrup et al. 2007). Beyond their contribution to macroscopic disease features, ciliates contribute to pathogenesis by actively ingesting Symbiodiniaceae along with coral tissue (Seveso et al. 2015, Sweet & Bythell 2012).

1.2.6. Skeletal eroding band disease. Skeletal eroding band disease is a widespread coral disease linked to another ciliate, *Halofolliculina corallasia*. Characterized by a slowly progressing black or dark gray band across the coral surface, this disease ultimately leads to progressive tissue loss (Winkler et al. 2004). It primarily affects corals from the Pocilloporidae and Acroporidae families

and exhibits high prevalence in the Great Barrier Reef (Willis et al. 2004) and incidence in the Caribbean (Page et al. 2015) and Hawaii (Palmer & Gates 2010), suggesting a global distribution. Winkler et al. (2004) speculated that the ciliate may opportunistically settle and establish on coral tissue that has been damaged, for example, by predation (Winkler et al. 2004). However, it is not clear whether the ciliate causes tissue loss or colonizes the denuded skeleton (Page & Willis 2008).

2. NONBACTERIAL PARTNERS AND THEIR ROLE IN CORAL DISEASE: SYMBIODINIACEAE AND VIRUSES

Diverse microorganisms are implicated directly or indirectly in coral diseases. Multicellular eukaryotes like fungi and trematodes can cause infections and are associated with worsening coral health (Aeby 2015, Ainsworth et al. 2017, Bray & Cribb 1989). However, the majority of studies concerning the etiology of coral diseases currently focus on three categories of potential pathogens: protists, bacteria, and viruses. Each of these groups represents a broad collection of genetic diversity, metabolisms, life histories, and potential mechanisms of disease. Below, we summarize evidence regarding how these groups are directly and/or indirectly associated with coral disease.

2.1. Symbiodiniaceae and Disease Resistance/Susceptibility

As the primary nutritional symbionts of stony corals, the Symbiodiniaceae play a fundamental role in colony health by providing photosynthetically derived carbon resources to their cnidarian animal hosts (Muller-Parker et al. 2015). Our understanding of the diversity and physiological contributions (e.g., thermotolerance) of Symbiodiniaceae lineages to coral holobionts has benefited from extensive research attention for decades (Davies et al. 2023). Given this, surprisingly few studies have tested the extent to which Symbiodiniaceae identity (e.g., species and lineage) influences coral holobiont disease resistance or susceptibility. At a minimum, it has been documented that mutualistic Symbiodiniaceae lineages can shift to parasitism under stressful environmental conditions (Baker et al. 2018, Sachs & Wilcox 2006), which could contribute to (or follow) disease states in the holobiont.

Some *Symbiodinium* lineages appear to be more parasitic than other genera. For example, in the Caribbean, *Symbiodinium* was correlated with yellow (diseased) tissue areas on Caribbean *Orbicella annularis*, *Orbicella faveolata*, and *Orbicella franksi* colonies exhibiting signs of yellow band disease (Toller et al. 2001). Similarly, in the Pacific, *Acropora cytherea* white syndrome and *Vibrio* were correlated with colonies that harbored a *Durusdinium* lineage (Rouzé et al. 2016). Another study also found that corals with signs of dark spot syndrome are less likely to harbor *Durusdinium* lineage symbionts (Correa et al. 2009), but it is unclear whether this is because *Durusdinium* lineages are selectively lost from tissues affected by dark spot syndrome or because harboring a *Durusdinium* lineage improves colony resistance to dark spot syndrome. Recently, increased susceptibility to (Klein et al. 2024) and severity of SCTLD have been correlated with harboring *Durusdinium* symbionts (Beavers et al. 2023).

However, issues remain in testing linkages between Symbiodiniaceae and coral disease. For most tissue loss diseases, lesion progress across colony surfaces is faster (e.g., on the order of hours to days) than Symbiodiniaceae are typically observed to shuffle in relative abundance or are typically lost from a coral colony (e.g., via a bleaching-type response over several weeks). Also, associations between Symbiodiniaceae and some diseases could potentially be obfuscated by phylogenomic and phylogeographic associations between the animals and their protist counterparts. The primary phylogenomic issue is that multiple coral species can be affected by the same apparent coral disease, but these different holobionts may tend to form associations with different

genera or lineages of dinoflagellate symbiont, making the disease susceptibility or resistance of a given symbiont lineage harder to detect (e.g., differences in dominant Symbiodiniaceae within *S. siderea* samples with and without signs of dark spot syndrome in Florida, USA, and the US Virgin Islands; Correa et al. 2009). This challenge is compounded by the fact that stony coral species vary in the flexibility and specificity of their symbioses with Symbiodiniaceae (Silverstein et al. 2012).

Bleaching, the mass loss of Symbiodiniaceae and/or its pigments, can also trigger (Brandt & McManus 2009) or halt (Brandt et al. 2021) the progression of coral diseases. During and after bleaching, coral metabolism and cell integrity are severely altered, which may leave bleached colonies more susceptible to disease. Conversely, for diseases initiated through infection or dysfunction of Symbiodiniaceae, bleaching could slow or halt disease progression by removing these symbionts from the colony.

2.2. The Good, the Bad, and the Ugly: Viral Roles in Coral Immunity and Disease

Microscopy and high-throughput sequencing technologies have revealed extensive morphological and genetic diversity of putative virus-like particles (VLPs) and genomic sequences associated with coral animal tissues and coral-associated Symbiodiniaceae and bacteria (Correa et al. 2021, van Oppen et al. 2009, Vega Thurber et al. 2017). Despite this, viruses are a relatively understudied component of coral disease. Viral impacts on colony health and functioning likely span the good (bolstering coral immune system function and disease resistance), the bad (direct antagonism as the etiological agents of disease), and the ugly (indirect contributions to disease through increases in the virulence of other microorganisms or through secondary infections) (**Figure 2**). This section highlights seminal works, key developments, and promising future directions in understanding viral contributions to coral holobiont diseases.

2.2.1. The good: viral contributions to the coral immune system. Viral infections of bacterial, archaeal, and eukaryotic microbial symbionts can shift their community compositions, affecting their physicochemical contributions to coral mucosal and tissue layers (Grasis 2017, Quistad et al. 2017). This virus-derived immunity mechanism is likely impactful within the coral surface mucus layer, since surface mucus acts as a physical buffer to the surrounding environment and is the site of first defense against pathogen invasion. In the coral surface mucus, phage:bacteria ratios can be ∼4.5-fold higher than corresponding ratios in the water column (Barr et al. 2013, Nguyen-Kim et al. 2015). It has been suggested that this enriched phage environment includes coral immunophages, or bacteriophages that directly contribute to the coral immune system via pathogen cell lysis. Recently, immunophages within the mucus of the coral *Oculina patagonica* were shown to be capable of infecting *Vibrio mediterranei*, an emerging pathogen that causes bacterial bleaching (Rubio-Portillo et al. 2014). These mucus-associated vibriophages are present at low abundance during ambient conditions but proliferate rapidly during warming periods if *V. mediterranei* invades the coral surface mucus. Viruses that predate on other pathogenic bacteria should also be tested for immunophage roles. For example, cyanophages could contribute to colony resistance to black band disease through immunophage activity since cyanobacteria are implicated in the disease (Buerger et al. 2019, Veglia et al. 2021).

Eukaryotic viruses—those infecting the coral itself, Symbiodiniaceae, or other eukaryotic symbionts—are also potentially capable of influencing coral immune properties (Weynberg et al. 2017a). In mice, latent (dormant infection state) herpesvirus infections confer protection from bacterial pathogens by priming the mouse immune system through upregulation of nonspecific immune-related genes (Barton et al. 2007). Interestingly, viruses exhibiting some similarities to

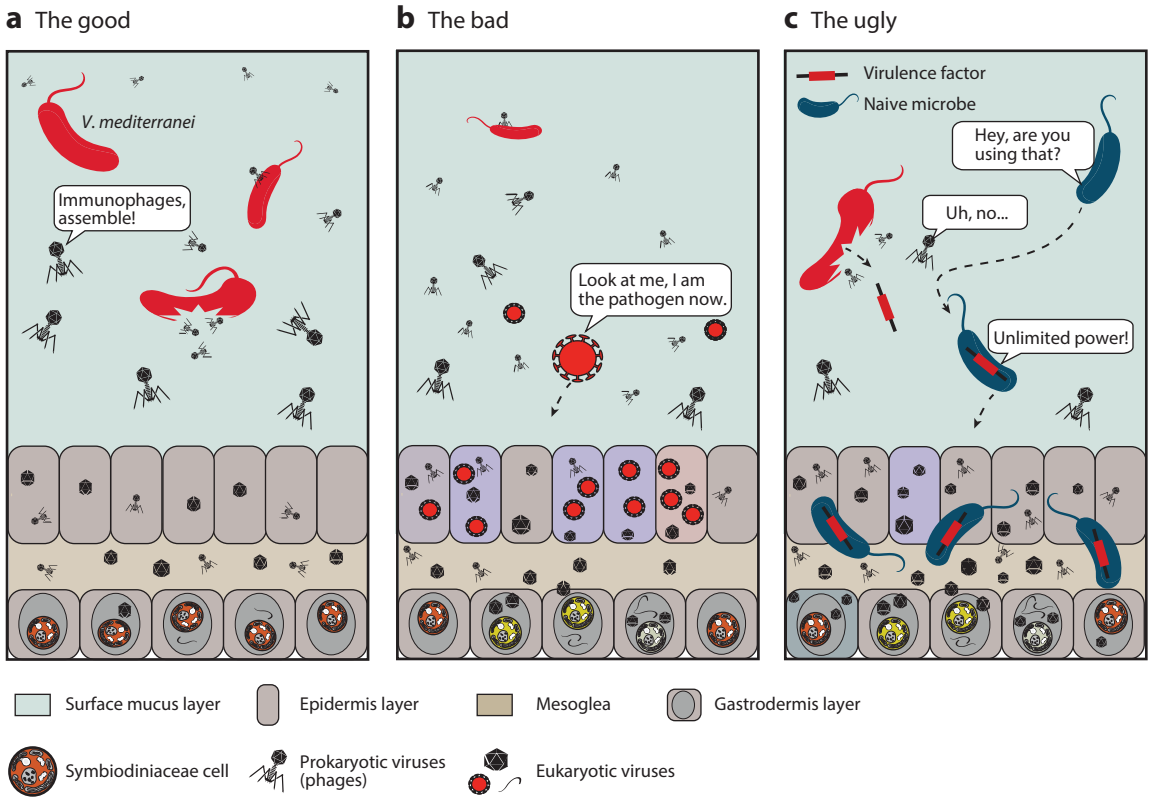

Figure 2

Viral impacts on colony health and disease, which likely span the good, the bad, and the ugly. (*a*) The good: Viruses may bolster coral immune properties in diverse ways, represented here as coral mucus-associated immunophages infecting *Vibrio mediterranei*, thereby countering pathogen invasion and maintaining holobiont homeostasis. (*b*) The bad: Viral infection of coral tissues or Symbiodiniaceae could initiate disease or bleaching signs in coral holobionts. Here, a pathogenic virus infects coral tissue, resulting in gross disease signs (represented by discoloration of coral epidermal cells) and increased production (secondary infections) by resident, latent, or chronic viruses. (*c*) The ugly: This scenario demonstrates the double-edged sword of immunophage activity. While immunophages effectively lyse invading pathogens, they also release bioavailable virulence factors. These genetic elements are then acquired by a nearby nonpathogenic microbe, transforming it into a new pathogen that invades coral tissues, again prompting secondary virus infections in the holobiont.

known Herpesviridae are common in stony coral holobionts (Correa et al. 2016, Vega Thurber et al. 2008, Wood-Charlson et al. 2015). It is hypothetically possible that latent atypical herpes-like virus infections can drive coral innate immunological priming and provide colonies with increased resilience to potential pathogens; this should be empirically tested. The identification of viral groups that contribute to or prime coral immune systems can support reef management by enabling targeted intervention efforts (see Section 4.2.2).

2.2.2. The bad: viruses as etiological agents of coral disease. A virus has yet to be confirmed as the etiological agent of a coral disease, or even comprehensively isolated, cultured, and characterized from diseased (or healthy) coral tissues or symbiont cells. However, for each coral disease in which viruses have been assessed (e.g., dark spot syndrome, white plague disease, white patch syndrome, SCTLD, tumors, and bleaching), diverse VLPs and apparent increases in viral production have been observed in stressed and unhealthy colonies (relative to apparently healthy

colonies, but see Wang et al. 2018). For example, higher abundances of Cressdnaviricota viruses were found in bleached and white plague–affected tissues relative to apparently healthy colonies (Soffer et al. 2013). Also, small (<50-nm diameter) icosahedral VLPs were significantly more abundant in coral tissues and Symbiodiniaceae 1 cm away from white patch lesions (Lawrence et al. 2015). Similarly, numerous studies have provided morphological and omics-based evidence that virus abundance or production increases in heat-stressed or bleached corals (Correa et al. 2016, Littman et al. 2011, Marhaver et al. 2008, Messyasz et al. 2020, Vega Thurber et al. 2009) and cultures of coral-associated Symbiodiniaceae (Weynberg et al. 2017b). These works suggest that viral infections play a role in coral disease, but additional evidence is needed to clarify whether viruses are the primary etiological agents.

Dinoflagellate-infecting RNA viruses (dinoRNAVs) are currently the most comprehensively investigated viral group in terms of potential contributions to coral bleaching signs. The genus *Dinornavirus* represents positive-sense, single-stranded RNA viruses that infect marine dinoflagellates (Tomaru et al. 2004). Currently, there is a single member of this genus (*Heterocapsa circularisquama* RNA virus), which infects the toxic bloom–forming dinoflagellate *H. circularisquama* (Tomaru et al. 2009). *Dinornavirus*-like sequences similar to *H. circularisquama* RNA virus were first detected in Caribbean coral tissues (Correa et al. 2013) from five sequences in thermally stressed *Montastraea cavernosa* RNA metaviromes and within transcriptomes from Symbiodiniaceae cell culture (genera *Symbiodinium* and *Breviolum*) (Bayer et al. 2012). In the decade since then, *Dinornavirus*-like sequences (dinoRNAVs) have been detected in the tissues of 12 Pacific coral species (Grupstra et al. 2022b; Howe-Kerr et al. 2023a,b; Montalvo-Proaño et al. 2017; Weynberg et al. 2014), the feces of two coral-eating fishes (Veglia et al. 2024), and additional transcriptomes from Symbiodiniaceae cell cultures (genus *Cladocopium*) (Levin et al. 2017). Additionally, dinoRNAV-like endogenous viral elements have been found in dinoflagellate genomes, which is strong evidence that Symbiodiniaceae are the target hosts of dinoRNAVs in coral colonies (Veglia et al. 2023).

The association of dinoRNAVs with Symbiodiniaceae, in combination with their similarity to a known dinoflagellate-infecting virus capable of lytic infection, suggests that dinoRNAVs may contribute to some coral bleaching signs. Grupstra et al. (2022b) observed a significant increase in dinoRNAV aminotype richness and dispersion within coral holobionts (*Pocillopora verrucosa–Cladocopium pacificum* and *Pocillopora ligulata–Cladocopium latusorum*) during an ex situ heat-stress experiment. This apparent temperature-driven dinoRNAV productivity was corroborated via the in situ characterization of dinoRNAV community dynamics associated with *Porites* cf. *lobata–Cladocopium* C15 across time and space, and before and after a thermal stress event, on a Pacific reef (Howe-Kerr et al. 2023a). Assessing dinoRNAV infection prevalence at the Symbiodiniaceae cell level (rather than the coral holobiont level) with single-cell RNA sequencing, double-stranded RNA immunofluorescence (Coy et al. 2023), or other approaches and correlating physiological shifts in individual Symbiodiniaceae cells with dinoRNAV infection will confirm the extent to which dinoRNAV infections lyse Symbiodiniaceae cells in heat-stressed coral tissues (as documented for other VLPs whose morphologies are similar to *Dinornavirus*'s; Davy et al. 2006, Wilson et al. 2001) and reveal the extent to which dinoRNAV infections contribute to coral bleaching signs.

2.2.3. Bad or just ugly? Direct versus indirect roles of viruses in stony coral tissue loss disease. Initial investigations of the etiology of SCTLD focused on bacterial diversity (see Section 1.2.1). However, a report of filamentous VLPs associated with Symbiodiniaceae cells in SCTLD-affected and unaffected Florida corals (Work et al. 2021) drove researchers to look more deeply into the role of viruses in this disease. Two novel Alphaflexiviridae genomes

[coral holobiont-associated alphaflexvirus 1 (CHFV1) and CHV2] were then generated from RNA sequencing libraries of US Virgin Island corals from SCTLD-affected, -exposed, and -unexposed colonies (Veglia et al. 2022). Detection of sequence similarities with positive-sense, single-stranded RNA viruses provided additional support for, but not confirmation of, the role of filamentous viruses in SCTLD.

The lack of data on coral holobiont-associated viral diversity for many host species, geographic locations, and disease states complicates the evaluation of viruses as potential etiological agents of disease. Except for one study documenting filamentous VLPs associated with white patch disease (Lawrence et al. 2015) and the documentation of filamentous VLPs in heat-stressed Symbiodiniaceae cultures (Weynberg et al. 2017b), putative filamentous viruses had not been significantly linked to coral disease. Yet examination of more than 700 transmission electron microscopy images of Symbiodiniaceae cells from apparently healthy and heat-stressed or bleaching corals in the Pacific subsequently revealed that filamentous VLPs are common and prevalent in an ocean basin where SCTLD has yet to be documented, making these viruses unlikely to be the sole etiological agent of this disease (Howe-Kerr et al. 2023b).

Upregulation of antiviral immunity genes in coral and Symbiodiniaceae from SCTLD-affected coral holobionts during an ex situ transmission experiment additionally implicated viruses in SCTLD etiology (Beavers et al. 2023). From the same samples, we documented differential abundance of various viral orders and found limited support for a single virus pathogen (i.e., CHFV). Importantly, however, similar viral orders were differentially abundant in SCTLD-affected corals analyzed from Floridian reefs based on identical methods (Vega Thurber & Correa 2023). Taken together, studies to date have informed hypotheses about viruses as potential etiological agents that can now be tested pending development of more quantitative sequence-independent virus detection approaches. Viruses that should be further investigated for "bad" roles include groups predicted to infect Symbiodiniaceae, such as Algavirales and Durnavirales, as well as potential coral-infecting viruses, including Herpesvirales and Chitovirales.

Another key finding that highlights potential "ugly" viral roles in some aspects of SCTLD was the observed upregulation of the gene *Abce1* (Beavers et al. 2023), a negative regulator of RNase L, a protein that has antiviral capacity via viral RNA degradation (Drappier & Michiels 2015). Importantly, upregulation of *Abce1* to inhibit RNase L is an antiviral evasion mechanism utilized by some human positive-sense, single-stranded RNA viruses, including one within Picornavirales (encephalomyocarditis virus) (Martinand et al. 1998). Picornavirales was also differentially abundant in SCTLD-affected tissues across all coral species analyzed by Vega Thurber & Correa (2023) and Veglia (2023) (Veglia et al. 2024). We thus hypothesize that the onset of SCTLD infection induces Picornavirales to employ antivirus evasion tactics, potentially undermining the coral's immune response to virus infection and enabling opportunistic production by diverse viral groups and, ultimately, holobiont destabilization.

3. CORAL DISEASE ECOLOGY, THE ENVIRONMENT, AND RESTORATION

Outside of the invasion and epidemic conditions of white band disease and SCTLD, environmental conditions are closely associated with coral disease incidence, prevalence, and severity. Increases in ocean temperatures associated with climate change are often positively correlated with coral disease dynamics and outbreak conditions (Maynard et al. 2015, Randall & van Woesik 2015). This phenomenon likely fuels different processes associated with disease dynamics by directly affecting the disease agent, promoting higher growth rates of pathogens (Ward 2006), triggering virulence pathways (Kimes et al. 2011), and/or causing coral physiological stress, resulting in a compromised immune system within the host (Brandt & McManus 2009, Miller et al. 2009). Although

coral disease outbreaks often follow or coincide with major stress events, such as coral bleaching episodes (Croquer & Weil 2009, Jones et al. 2004, Weil et al. 2009a), they are not necessarily a direct result of high temperatures per se; rather, they arise because the coral hosts have lost their algal symbiont partners and are then compromised in health and immunity (Mydlarz et al. 2009, Pinzón et al. 2015).

Experimental manipulations within the field and laboratory show that nutrient enrichment also increases coral disease prevalence and severity (Bruno et al. 2003, Vega Thurber et al. 2014, Voss & Richardson 2006). However, whether nutrients affect the disease agents directly, further compromise the coral hosts, or both is largely unknown. One area that has been well studied, however, is the effects of nutrients on *Aquarickettsia rohweri*, a hypothesized intracellular parasite of the critically endangered coral *Acropora cervicornis*. Elevated nutrients promote the abundance of *A. rohweri* within the coral hosts, ultimately reducing growth and increasing disease susceptibility (Klinges et al. 2022, 2023). As coral diseases are also often more common within urbanized areas with poor water quality or areas with elevated direct human impact, it is likely that the severity of coral diseases will continue to increase, directly and indirectly, as a consequence of persistent global eutrophication (Malone & Newton 2020).

3.1. Coral Restoration and Coral Disease Dynamics

Coral restoration has become a common strategy to assist the recovery of reef-building corals in anticipation of the return of reef ecosystem function across bioregions, particularly in the Caribbean. Coral diseases have therefore become an accelerating factor of observed trends of homogenizing reef communities and reef flattening recorded across the Caribbean. In addition to the direct benefits associated with reseeding a reef with living coral tissue, restoration efforts have indirectly facilitated and accelerated coral disease research. Although coral restoration has advanced coral disease research, particularly within endangered coral species like Caribbean acroporids, persistent acute and chronic disease incidences within the reef environment continue, limiting the efficacy of coral restoration initiatives (Miller et al. 2014).

A major objective of many restoration initiatives focuses on creating reproductively viable corals within a few years or less after outplanting (Koch et al. 2022b) to assist with jump-starting population recovery. Coral disease epizootic events can cause complete colony mortality of outplanted corals within short periods of time but can also result in partial mortality of large, established outplants in land-based facilities and in situ coral nurseries, thus reducing the ability of these corals to sexually reproduce (Weil et al. 2009b) and reducing the efficacy of long-term restoration activities. Restoration efforts may also increase the likelihood of disease epizootic events for pathogenic agents that are density dependent. Currently, many of the endemic diseases within the Caribbean occur spatially at random within reef scales (Foley et al. 2005, Muller & van Woesik 2012, Zvuloni et al. 2009), and disease occurrences may be associated with ubiquitous dormant pathogens that become pathogenic when the host's immunity becomes compromised following a dysbiosis within the host microbiome (MacKnight et al. 2021). However, these random distributions are often observed within reefs that are already depauperate of coral hosts, and diseases may become more clustered as host density within reefs increases, allowing for greater intercolony transmission over small spatial scales. The manipulation of outplanting strategies to test for density dependence within coral disease dynamics of these restoration sites should be a research priority for restoration programs. Additionally, disease management is likely a critical component to any successful restoration plan and likely must include innovative novel approaches to reduce both inter- and intracolony disease transmission within outplanted corals (e.g., see Section 4).

From a coral implementation perspective, coral diseases affect the capacity to harvest corals, as the production of sexual coral spats and microfragments can be significantly reduced when either parental or donor colonies are scarce after massive mortalities. Coral diseases can therefore alter, delay, or even hinder the outcomes of a coral restoration and increase the costs as mortality spreads out across reefs in nurseries and land-based facilities.

3.2. Integration of Coral Immunity, Microbiology, Stress Dynamics to Understand Disease Susceptibility

Disease susceptibility is caused by a combination of factors, including the genetics of the hosts and potential pathogens, the immunological and physiological status of all the holobiont members, and the prevailing environmental conditions (e.g., temperature, salinity, sedimentation, and nutrient concentrations). Coral genotype has clear roles in disease susceptibility. At the same time, coral immunology varies among coral taxa, and this variation has long been suspected to play an important role in the relative disease susceptibility of coral species. Yet all of these intersecting parts of the disease puzzle matter for understanding coral disease onset, progress, and culmination. For example, the levels of some immune parameters are correlated with disease susceptibility and bleaching mortality across 10 cnidarian families (Palmer et al. 2010). Surveys of immunity, surface microbiomes, and disease on the Great Barrier Reef revealed that increased microbiome variability, reduced microbiome diversity, and lowered immune activity precede signs of white syndrome among corals (Pollock et al. 2019).

In addition to the direct effects of immune variation on susceptibility to pathogens, there are also likely to be indirect effects resulting from immunity-driven modifications to coral–microbial symbiosis, which in turn influence disease susceptibility. For example, in *Hydra*, the antimicrobial neuropeptide NDA-1 promotes establishment of *Curvibacter* sp. during development by suppressing gram-positive bacterial growth (Augustin et al. 2017). In association with either *Acidovorax* sp. or *Pseudomonas* sp. microbes, *Curvibacter* in turn protects *Hydra* against infections by *Fusarium* fungi (Fraune et al. 2014). Evidence is emerging that similar mechanisms may exist in corals. Transcriptomic studies often see differences in innate immune gene expression. For example, SCTLD-infected corals differed in their expression of 30 innate immune genes (Beavers et al. 2023), including three members of the NF-κB pathway (*smad6*, *TLR6*, and *Traf3*). *Dmbt1*, which plays a role in mucosal innate immunity, notably fell in expression during SCTLD infection, concurrently with disruption to the mucosal microbiome of SCTLD. Thus, pathogen infection may alter innate immune gene expression, which in turn may potentially further alter microbiome structure (Mohamed et al. 2023, Voolstra et al. 2024). It is important to emphasize that the microbiome may be able to remember past encounters with pathogens or environmental stressors, known as microbiome memory, as shown by Vompe et al. (2024). Epigenomic modifications may mediate this memory. These modifications allow the microbiome to anticipate and respond more effectively to future challenges, potentially enhancing resilience to infection (Mohamed et al. 2023). On the other hand, the adapted microbiome may potentially interfere negatively with the host interaction.

Importantly, not all symbiotic interactions are equal. It is well established that factors like environmental stress, coral immunity, pathogen infection, and macroalgal competition can alter coral microbiome structure and biodiversity, which may have secondary consequences for disease susceptibility. Critically, many of these factors also have the potential to change the nature of host–microbial symbiosis—converting friend into foe or harmless neighbor into dire threat (**Figure 3**). The most obvious example of this type of shift in the nature of symbiotic interactions is the change in symbiosis between coral hosts and their dinoflagellate partners, Symbiodiniaceae, which breaks down during thermal stress, resulting in inorganic nutrient and carbon metabolism

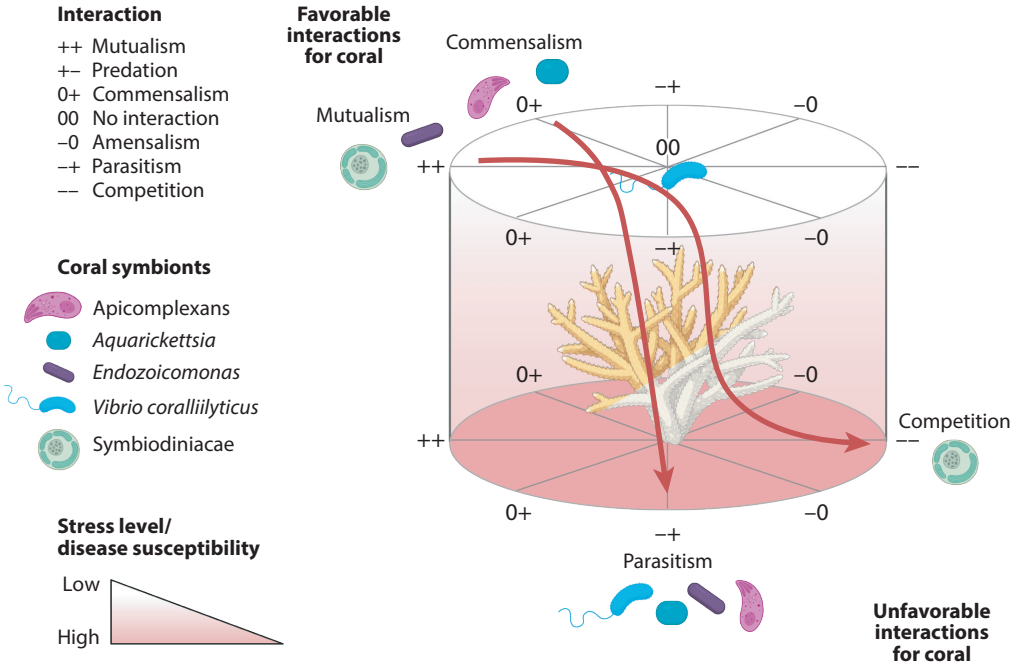

Figure 3

Changes in symbiosis during disturbance that move from favorable to unfavorable interactions. Symbiotic interactions between corals and microbes can range from mutualism to competition, with environmental stress having the potential to shift the nature of those interactions. The cylinder indicates symbiotic interactions and their fitness consequences for the host (*first symbols*) and symbiont (*second symbols*). For example, – + indicates parasitism by a symbiont (which reduces coral fitness but increases symbiont fitness), whereas + – indicates predation of a symbiont by the host (*legend*). The paths traced by arrows show how moving from environmental conditions that are ideal for the coral (*top of cylinder*) to stressful for the coral (*bottom of cylinder*) can shift symbiotic interactions toward predation of or competition with the host (*arrows*).

imbalances (Rädecker et al. 2023), redox fluctuations (Nielsen et al. 2018), and potential bleaching (Helgoe et al. 2024). If this essential nutritive mutualism is not reestablished, its loss results in disease and the death of the holobiont. At the same time, during this breakdown, corals may actually predate upon their symbionts, scavenging their once mutualist partners for needed nutrition (Wiedenmann et al. 2023). Thus, this relationship has moved from one of shared benefit to competition and predation.

Further, if variations in coral microbiomes within populations correspond to variations in disease susceptibility (coral species vary greatly in microbiome composition, richness, evenness, and membership), then some of the large differences in overall disease susceptibility among coral species may also be due to the evolution of microbial symbiosis. Indeed, a recent comparison of coral microbiomes across 40 coral genera suggested that a substantial fraction of genus-to-genus differences in coral disease susceptibility correspond to the abundance of *Endozoicomonas* in coral tissues (Epstein et al. 2023). This result appears paradoxical, as *Endozoicomonas* is commonly lost during coral disease and becomes more abundant after thermal stress in amplicon surveys. The same study, however, observed that *Endozoicomonas* also correlates with coral growth rate. Thus, association with *Endozoicomonas* may influence life-history strategy by promoting faster growth but at the cost of increased vulnerability to disease (Epstein et al. 2023). In other words, although *Endozoicomonas* is often considered a mutualist, it may contribute to disease under various unfavorable environmental scenarios (Pogoreutz & Ziegler 2023).

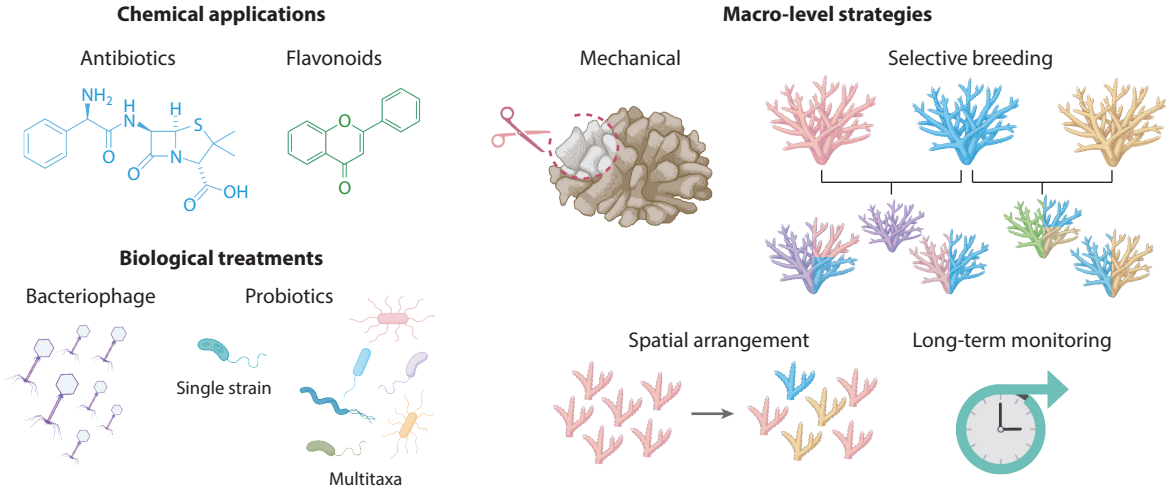

Figure 4

Innovative approaches to preventing and mitigating coral disease. This figure depicts the three direct disease intervention approaches employed to manage coral disease: chemical applications (*top left*), biological treatments (*bottom left*), and macro-level strategies (*right*).

4. INNOVATIVE APPROACHES TO MANAGING CORAL DISEASE

Therapies to treat sick corals and preventative measures to avert disease onset and transmission are limited. Below, we discuss the three main approaches employed by restoration managers and researchers to treat diseased lesions: chemical applications, biological methods, and macro-level strategies. No one approach has proven to be a panacea for coral disease treatment, but together they have the potential to aid in generating healthier and more resilient coral reefs (**Figure 4**).

4.1. Chemical Applications for Disease Prevention and Intervention

Chemical applications are commonly employed against human, animal, and agricultural diseases. Their use in corals, while not widely adopted, has resulted in mixed results and efficacies. In general, antiseptics like chlorinated epoxy have been highly ineffective in treating diseased corals (Neely et al. 2021, Walker et al. 2021), with the exception of one study on black band disease in Hawaii (Aeby et al. 2015). Antibiotics, on the other hand, have shown more promise in treating multiple diseases at the individual level. Broad-spectrum antibiotics are attractive treatments for corals, as the majority of disease-causing agents are either unknown or driven by multiple diverse taxa. Notably, the antibiotic amoxicillin has been successful in treating SCTLD-affected corals. Applying a combination of amoxicillin and Base 2B, a silicone product to prevent antibiotic leaching, can quickly halt SCTLD lesion progression (Shilling et al. 2021), although its effectiveness appears to be coral species specific (Forrester et al. 2022, Lee Hing et al. 2022, Studivan et al. 2023). While amoxicillin does not prevent new lesions from appearing on a given coral, halting disease progression through initial treatments is predicted to decrease reinfection, allowing reef sites to progress to lower SCTLD prevalence (Neely et al. 2021). Notably, this same treatment is effective in treating *Pseudodiploria* spp. infected with black band disease in the US Virgin Islands (Eaton et al. 2022).

A critical issue for all antibiotics is the potential development of antibiotic resistance and its implications for nearby species and the surrounding environment. Antibiotic resistance occurs when targeted microbes no longer respond, rendering infections difficult to treat and increasing the risk

of disease spread. Even diluted concentrations of antibiotics allow bacterial populations to develop defensive mechanisms that inhibit antibiotic function (Jutkina et al. 2018). The emergence of antibiotic-resistant pathogens has had a global effect, reverberating across diverse ecosystems. For example, *Serratia marcescens*, the pathogen responsible for acroporid serratiosis (white pox) in *Acropora palmata*, has become resistant to a wide range of antibiotics as a consequence of exposure to antibiotics used to treat *Serratia* infections in humans (Tavares-Carreon et al. 2023).

While the use of antibiotics in coral ecosystems has raised concerns, it is important to recognize the dual role that antibiotics can play in coral health management. Beyond their direct therapeutic applications, antibiotics hold promise as diagnostic tools for identification and selection of appropriate treatments for coral diseases (Kline & Vollmer 2011, Sweet et al. 2014). Antibiotics, when strategically applied, can help isolate and identify specific pathogens involved in coral ailments. This targeted approach paves the way for tailored and effective treatment regimens but cannot differentiate between primary and secondary disease agents. Researchers treating coral disease with amoxicillin are rightly concerned about the unintended long-term consequences of antibiotic treatments in the marine environment. To minimize this risk, practitioners apply highly concentrated dosages of amoxicillin that kills pathogens, commensals, and underlying coral tissue (Walker et al. 2021). This type of application is less likely to lead to antibiotic resistance than successive low-dosage treatments (Roberts et al. 2008).

Other chemical applications also warrant examination. For example, flavonoids are polyphenolic phytochemicals that are commonly found in marine organisms, including corals (Martins et al. 2019), and have natural bactericidal, bacteriostatic, antiviral, and antiprotozoa properties (Martínez-Castillo et al. 2018). One study found that *Sargassum* extracts, including flavonoids, are inhibitory to coral pathogen cultures (Ahmed et al. 2022). The efficacy of flavonoids in combating plant diseases and their proposed use as substitutes for antibiotics in human health (Biharee et al. 2020) imply that these compounds are promising options for addressing coral diseases that should be explored.

4.2. Biological Treatments for Disease Mitigation: Probiotics and Bacterial Predators

Biological agents are emerging as potentially powerful tools to treat coral disease. This antibiotic-independent therapy can employ a single beneficial taxon or a consortium of microbes and has the potential to act beyond a single inoculation or individual coral colony and distribute at the reef scale, and has thus gained traction in recent years. The specificity of these biological agents depends on the chosen taxa and can range from highly specific to broad acting.

4.2.1. Beneficial microorganisms for corals and probiotics to prevent and ameliorate disease. The microbes involved in biological treatments are commonly called beneficial microorganisms for corals (BMCs): consortia of naturally associated coral microorganisms that contribute to host health (Peixoto et al. 2017). BMCs can function as probiotics, providing health benefits when administered in appropriate doses (Peixoto et al. 2021). BMCs are typically isolated from healthy corals that have a desired phenotype, such as elevated disease resistance or wider thermal tolerance compared with their congeners, and then reinoculated into unhealthy corals or those with inferior traits. By employing multiple taxa simultaneously, these therapies can promote coral health through multiple mechanisms, including enhancing host immune response, creating direct antagonism against pathogens, excluding invaders through indirect niche colonization, and contributing to nutrient cycling. One study found that the addition of five putatively beneficial coral microbes mitigated *Vibrio coralliilyticus*–induced bleaching in *Pocillopora damicornis* (Rosado et al. 2019).

BMC studies have focused primarily on improving coral resilience and acting as preventative rather than curative treatments for pathogen-mediated diseases. For example, BMCs can mitigate temperature-induced bleaching (Doering et al. 2021, Li et al. 2023, Rosado et al. 2019, Santoro et al. 2021) and improve host physiology (Zhang et al. 2021). While studies applying BMCs as probiotics are in early stages, the observed advantages indicate the need for future investigations into the potential of these treatments for disease prevention and/or mitigation. Inoculated BMCs are not retained within host microbiomes for long periods and demonstrate optimal efficiency when applied during stress (Voolstra et al. 2021). Therefore, use of these treatments would likely require readministration at times of stress, although there might be epigenetic elements to be further considered for long-term benefits that are independent of the probiotic retention. Management actions that bolster natural processes (e.g., trophic transmission) that spread BMCs on reefs may be key to achieving scalability (Barno et al. 2021, Grupstra et al. 2022a).

Single-taxon BMCs also show promise as antibiotic-independent treatments for coral disease. They aim to prevent disease via direct antagonism of pathogens and opportunists without compromising the integrity of the coral holobiont and other bacteria in the coral surface mucus layer, which may defend the holobiont against foreign invaders. These applications are among the least explored methods to combat coral disease, yet early studies have demonstrated their effectiveness as treatments and preventatives (prophylactics) without substantially altering the composition of coral microbiomes. Coral isolates with antibiotic and/or antagonistic activity toward coral pathogens have been identified and tested in vitro (Deutsch et al. 2022, Sweet et al. 2021), and several strains have been tested in vivo. A recent study implemented a *Pseudoalteromonas* species (strain MCH1-7) as a probiotic to treat SCTLD-infected *M. cavernosa* (Ushijima et al. 2023). MCH1-7 has broad-spectrum antibacterial activity and was able to arrest or slow disease progression in treated corals, as well as prevent disease transmission to untreated corals.

Another potential single-taxon probiotic is a less commonly studied microbial predator of coral bacteria, *Halobacteriovorax*. Originally identified in coral microbiomes during experimental stress experiments (Vega Thurber et al. 2009), subsequent application studies of *Halobacteriovorax* prevented *V. coralliilyticus*–induced infection without affecting other microbiome members in stressed *M. cavernosa*, suggesting that bacterial predators may mitigate the ability of pathogens to cause disease outbreaks (Welsh et al. 2016, 2017). Because these organisms predate on a large variety of blooming bacteria and are natural, low-abundance members of coral microbiomes, *Halobacteriovorax* treatments could be a viable and safe option to combat the coral disease epidemic, particularly in nursery settings.

Testing probiotic efficacy requires further development of coral disease models to test new therapies and efforts to address the scalability of biological treatment strategies on a reef-wide scale. Emphasis should be placed on identifying delivery mechanisms that facilitate a gradual release of probiotics over time, reduce the frequency of required treatments, and promote treatment spread across the entire reef following the inoculation of a limited number of coral colonies.

4.2.2. Phage therapy for bacterial diseases. In this review, we also consider viruses as biological treatments, given their similar mode of action to other biological agents and distinction from chemical and mechanical treatments. Phage therapy employs bacteriophages, the viruses of bacteria, as highly specific targets for a single pathogen (even at the strain level) and can be effective when etiological agents are well defined. Although the majority of coral diseases do not have well-defined disease-causing agents, a causal relationship between a bacterium and a particular coral disease has only been established for a few bacterial taxa. Bacteriophages specific to *V. coralliilyticus*, which causes tissue loss and bleaching in a range of coral species, and *Thalassomonas loyana*, the cause of plague-like lesions in *Favia favus*, have been effective in both tank and field

experiments (Cohen et al. 2013, Efrony et al. 2009, Jacquemot et al. 2018, Kim et al. 2019). The timing surrounding phage addition appears to be crucial for successfully preventing coral disease. For example, *T. loyana* phage BA3 successfully prevented tissue loss and death in corals that were treated within one day after infection by *T. loyana* but was ineffective if applied after two days (Efrony et al. 2009).

As with antibiotics, the development of phage resistance is a significant barrier to effective phage therapy implementation, although its use is not associated with spread resistance to other pathogens and ecosystems due to its highly targeted nature. Phage resistance can occur rapidly; phage-resistant members of the target population have occurred in up to 80% of biomedical studies treating intestinal diseases (Oechslin 2018). However, some of the mutations that confer phage resistance can reduce pathogen virulence. Therefore, phage therapy may have the capacity to reduce disease spread and severity even while promoting phage resistance. For coral diseases specifically, phage therapy may address many problems of scaling. Some phage have high replication rates and large burst sizes, meaning that only a small concentration of viral particles is necessary to inoculate a diseased lesion and expand throughout coral tissue. Further, studies examining the efficacy of phage against coral disease and the long-term consequences of these treatments for treated corals and the reefs they inhabit are needed to determine the feasibility of this treatment in vivo.

4.3. Macro-Level Strategies for Disease Prevention and Mitigation

In combination with chemical and biological treatments, effective macro-level strategies are paramount for mitigating coral diseases (NASEM 2019). Macro-level strategies range from mechanical treatments, to selective breeding for more disease resistant coral holobionts, to broader approaches aimed at preventing coral disease. Mechanical treatments involve removing diseased tissue, performing debridement, smothering diseased lesions, or creating trenches to prevent lesion spread and are often used in combination with chemical approaches. These strategies are rarely successful in isolation (Miller et al. 2014), as etiological agents can exist in both diseased and healthy coral tissue as well as in free-living cells in the water column. Moreover, their reliance on an extensive amount of manpower renders them unsustainable for most diseases.

Long-term strategies such as selective breeding and long-term monitoring are necessary to stop the global increase in coral disease prevalence and spread. For instance, ongoing restoration initiatives aimed at identifying and cultivating disease-resistant coral genotypes contribute significantly to curbing the spread of infectious diseases on reefs (Kiel et al. 2023, Klepac et al. 2024, Koch et al. 2022a). In addition to propagating taxa that are less susceptible to disease, these efforts increase the genetic diversity of corals throughout all steps of restoration, from propagating coral fragments in nurseries to outplanting corals on reefs. These efforts aim to fight the monoculture effect (Altermatt & Ebert 2008), which can lead to unsustainable long-term environments that build up disease pressure. For instance, ongoing coral restoration initiatives aimed at identifying and cultivating disease-resistant coral genotypes contribute significantly to curbing the spread of infectious diseases on reefs. Enhancing the prevalence of disease-resistant genotypes on a reef reduces the overall pathogen load and makes pathogen transmission less likely, similarly to the protective effect of vaccination at the population level. This proactive approach not only safeguards disease-susceptible corals but also bolsters the overall resilience of the reef. Similar disease-independent research initiatives have found that crossbreeding corals of the same species across latitudes can promote heat tolerance (Dixon et al. 2015).

Increasing the genetic diversity of coral fragments during restoration, coupled with strategic spatial arrangement, has proven to be effective in constraining disease outbreaks. Drawing insights from terrestrial systems, researchers recently demonstrated a notable positive correlation

between the diversity of *A. cervicornis* coral fragments on frames in nurseries and their resistance to disease. Frames exhibiting higher genetic diversity had elevated overall resistance to disease compared with frames with a single coral genotype (Brown et al. 2022). Implementing this approach offers a relatively cost-effective strategy to reduce disease susceptibility resistance by distributing pathogens across nonviable hosts.

5. A GLOBAL PERSPECTIVE ON WHAT WE NEED NEXT

Further research must be done to understand how coral diseases originate, what genetic factors make a coral more or less susceptible to disease, how diseases spread between individuals and between reefs, and how disease prevalence is influenced by reef composition and other environmental factors. Undertaking this work will demand significant time and financial resources, yet the costs of this comprehensive work are justified by the precipitous ongoing decline of reefs globally. Ultimately, we have learned a remarkable amount about diseases of corals but not enough to limit and mitigate their impacts. SCTLD exemplifies how a disease epizootic can devastate already threatened and at-risk species.

To control coral disease outbreaks, as a society we must use all available strategies that span scales across time and space (**Figure 5**) to slow down and if possible reverse climate change, while also mitigating local pollution and eutrophication (Gove et al. 2023). Thermal stress and synergistic local impact pressures will otherwise continue to decimate shallow-water coral populations directly via bleaching and mortality and/or indirectly through stress-mediated disease events. Agencies need to work together to fund research and create cross-program task forces

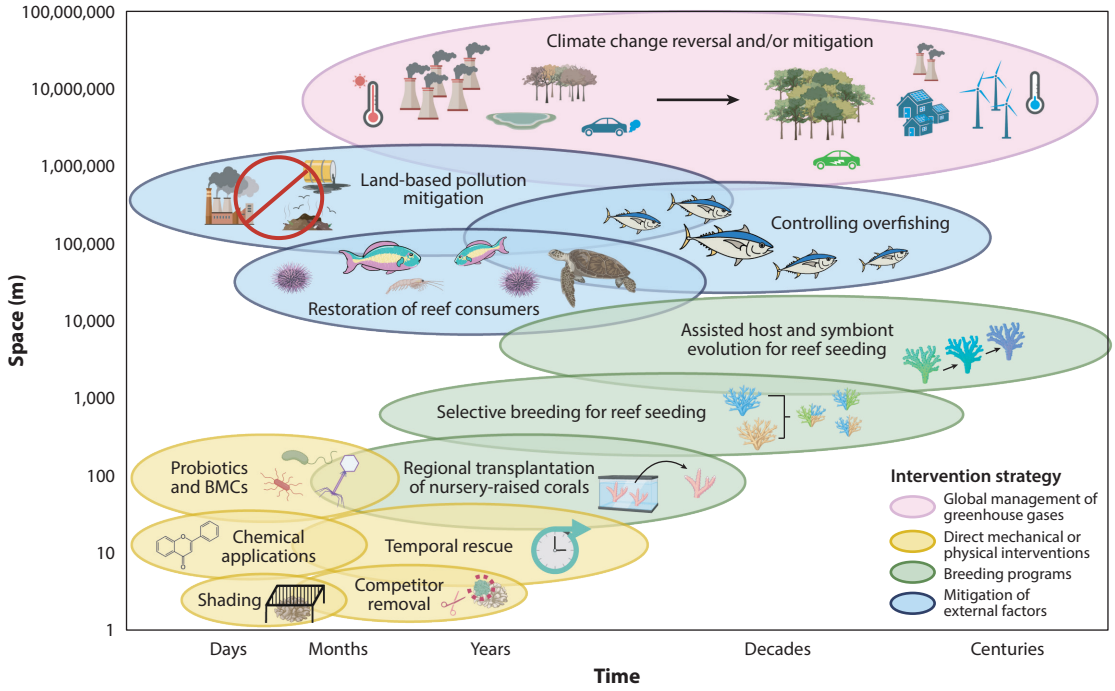

Figure 5

Holistic approach and scaling issues in coral disease management. This Stommel diagram shows the time (*x* axis) and space (*y* axis) scales for disease management strategies. The oval colors indicate the type of intervention strategy. Abbreviation: BMC, beneficial microorganism for corals.

to understand the causes and consequences of disease epizootics. An excellent example in the United States is the multi-agency-led Disease Advisory Committee (DAC), an SCTLD-focused task force that has mobilized scientists, managers, and funding to understand and monitor this disease, particularly in Florida but also across the Caribbean. The Florida DAC has been utilized as a framework for other geographies, such as the US Virgin Islands and Puerto Rico DACs. These existing task forces have laid out response plans and lessons learned that can be utilized by other nations should SCTLD spread into other regions, including the Pacific.

Innovative approaches to disease mitigation should be encouraged, and restoration programs must receive continued support and investment. In the Caribbean, restoration efforts should focus on two aspects: (*a*) restoring, rehabilitating, or enhancing population numbers for species that have been severely affected by SCTLD and/or driven near to extinction and (*b*) accounting for and propagating genotypes resistant and/or immune to SCTLD, bleaching, and other health problems via assisted coral reproduction while ensuring that coral populations remain genetically diverse. Continuous monitoring programs, such as tracking tagged colonies that survive and/or resist SCTLD and/or other compromised health problems, are critical to informing coral assisted reproduction, propagation, and restoration efforts. All efforts have risks, but the biggest risk is to do nothing at all.

DISCLOSURE STATEMENT

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LITERATURE CITED

Aeby GS. 2015. Porites trematodiasis. In *Diseases of Coral*, ed. CM Woodley, CA Downs, AW Bruckner, JW Porter, SB Galloway, pp. 387–90. Hoboken, NJ: Wiley & Sons

Aeby GS, Work TM, Runyon CM, Shore-Maggio A, Ushijima B, et al. 2015. First record of black band disease in the Hawaiian archipelago: response, outbreak status, virulence, and a method of treatment. *PLOS ONE* 10(3):e0120853

Ahmed N, Mohamed HF, Xu C, Sun X, Huang L. 2022. Novel antibacterial activity of *Sargassum fusiforme* extract against coral white band disease. *Electron. J. Biotechnol.* 57:12–23

Ainsworth TD, Fordyce AJ, Camp EF. 2017. The other microeukaryotes of the coral reef microbiome. *Trends Microbiol.* 25(12):980–91

Ainsworth TD, Kramasky-Winter E, Loya Y, Hoegh-Guldberg O, Fine M. 2007. Coral disease diagnostics: What's between a plague and a band? *Appl. Environ. Microbiol.* 73(3):981–92

Altermatt F, Ebert D. 2008. Genetic diversity of *Daphnia magna* populations enhances resistance to parasites. *Ecol. Lett.* 11(9):918–28

Alvarez-Filip L, González-Barrios FJ, Pérez-Cervantes E, Molina-Hernández A, Estrada-Saldívar N. 2022. Stony coral tissue loss disease decimated Caribbean coral populations and reshaped reef functionality. *Commun. Biol.* 5(1):440

Andersson ER, Stewart JA, Work TM, Woodley CM, Schock TB, Day RD. 2020. Morphological, elemental, and boron isotopic insights into pathophysiology of diseased coral growth anomalies. *Sci. Rep.* 10(1):8252

Aronson RB, Precht WF. 2001. White-band disease and the changing face of Caribbean coral reefs. *Hydrobiologia* 460(1):25–38

Augustin R, Schröder K, Murillo Rincón AP, Fraune S, Anton-Erxleben F, et al. 2017. A secreted antibacterial neuropeptide shapes the microbiome of *Hydra*. *Nat. Commun.* 8(1):698

Baker DM, Freeman CJ, Wong JCY, Fogel ML, Knowlton N. 2018. Climate change promotes parasitism in a coral symbiosis. *ISME J.* 12(3):921–30

Barno AR, Villela HDM, Aranda M, Thomas T, Peixoto RS. 2021. Host under epigenetic control: a novel perspective on the interaction between microorganisms and corals. *BioEssays* 43(10):e2100068

Barr JJ, Youle M, Rohwer F. 2013. Innate and acquired bacteriophage-mediated immunity. *Bacteriophage* 3(3):e25857

Barton ES, White DW, Cathelyn JS, Brett-McClellan KA, Engle M, et al. 2007. Herpesvirus latency confers symbiotic protection from bacterial infection. *Nature* 447(7142):326–29

Bayer T, Aranda M, Sunagawa S, Yum LK, Desalvo MK, et al. 2012. *Symbiodinium* transcriptomes: genome insights into the dinoflagellate symbionts of reef-building corals. *PLOS ONE* 7(4):e35269

Beavers KM, Van Buren EW, Rossin AM, Emery MA, Veglia AJ, et al. 2023. Stony coral tissue loss disease induces transcriptional signatures of in situ degradation of dysfunctional Symbiodiniaceae. *Nat. Commun.* 14(1):2915

Biharee A, Sharma A, Kumar A, Jaitak V. 2020. Antimicrobial flavonoids as a potential substitute for overcoming antimicrobial resistance. *Fitoterapia* 146:104720

Borger JL. 2005. Dark spot syndrome: a scleractinian coral disease or a general stress response? *Coral Reefs* 24(1):139–44

Bosch TCG, Miller DJ. 2016. Introduction: the holobiont imperative. In *The Holobiont Imperative: Perspectives from Early Emerging Animals*, pp. 1–10. Vienna: Springer

Bourne DG, Ainsworth TD, Pollock FJ, Willis BL. 2015. Towards a better understanding of white syndromes and their causes on Indo-Pacific coral reefs. *Coral Reefs* 34(1):233–42

Bourne DG, Boyett HV, Henderson ME, Muirhead A, Willis BL. 2008. Identification of a ciliate (Oligohymenophorea: Scuticociliatia) associated with brown band disease on corals of the Great Barrier Reef. *Appl. Environ. Microbiol.* 74(3):883–88

Brandt ME, Ennis RS, Meiling SS, Townsend J, Cobleigh K, et al. 2021. The emergence and initial impact of stony coral tissue loss disease (SCTLD) in the United States Virgin Islands. *Front. Mar. Sci.* 8:715329

Brandt ME, McManus JW. 2009. Disease incidence is related to bleaching extent in reef-building corals. *Ecology* 90(10):2859–67

Bray RA, Cribb TH. 1989. Digeneans of the family Opecoelidae Ozaki, 1925 from the southern Great Barrier Reef, including a new genus and three new species. *J. Nat. Hist.* 23(2):429–73

Brown AL, Anastasiou D-E, Schul M, MacVittie S, Spiers LJ, et al. 2022. Mixtures of genotypes increase disease resistance in a coral nursery. *Sci. Rep.* 12(1):19286

Bruckner AW. 2015. History of coral disease research. In *Diseases of Coral*, ed. CM Woodley, CA Downs, AW Bruckner, JW Porter, SB Galloway, pp. 52–84. Hoboken, NJ: Wiley & Sons

Bruckner AW, Bruckner RJ. 2006. Consequences of yellow band disease (YBD) on *Montastraea annularis* (species complex) populations on remote reefs off Mona Island, Puerto Rico. *Dis. Aquat. Organ.* 69(1):67–73

Bruno JF, Petes LE, Harvell CD, Hettinger A. 2003. Nutrient enrichment can increase the severity of coral diseases. *Ecol. Lett.* 6(12):1056–61

Buerger P, Weynberg KD, Wood-Charlson EM, Sato Y, Willis BL, van Oppen MJH. 2019. Novel T4 bacteriophages associated with black band disease in corals. *Environ. Microbiol.* 21(6):1969–79

Bythell J, Pantos O, Richardson L. 2004. White plague, white band, and other "white" diseases. In *Coral Health and Disease*, ed. E Rosenberg, Y Loya, pp. 351–65. Berlin: Springer

Cervino J, Goreau TJ, Nagelkerken I, Smith GW, Hayes R. 2001. Yellow band and dark spot syndromes in Caribbean corals: distribution, rate of spread, cytology, and effects on abundance and division rate of zooxanthellae. *Hydrobiologia* 460(1):53–63

Chimetto Tonon LA, Thompson JR, Moreira APB, Garcia GD, Penn K, et al. 2017. Quantitative detection of active vibrios associated with white plague disease in *Mussismilia braziliensis* corals. *Front. Microbiol.* 8:2272

Clark AS, Williams SD, Maxwell K, Rosales SM, Huebner LK, et al. 2021. Characterization of the microbiome of corals with stony coral tissue loss disease along Florida's coral reef. *Microorganisms* 9(11):2181

Cohen Y, Pollock JF, Rosenberg E, Bourne DG. 2013. Phage therapy treatment of the coral pathogen *Vibrio coralliilyticus*. *MicrobiologyOpen* 2(1):64–74

Cooney RP, Pantos O, Le Tissier MDA, Barer MR, O'Donnell AG, Bythell JC. 2002. Characterization of the bacterial consortium associated with black band disease in coral using molecular microbiological techniques. *Environ. Microbiol.* 4(7):401–13

Correa AMS, Ainsworth TD, Rosales SM, Thurber AR, Butler CR, Vega Thurber RL. 2016. Viral outbreak in corals associated with an in situ bleaching event: atypical herpes-like viruses and a new megavirus infecting *Symbiodinium*. *Front. Microbiol.* 7:127

Correa AMS, Brandt ME, Smith TB, Thornhill DJ, Baker AC. 2009. *Symbiodinium* associations with diseased and healthy scleractinian corals. *Coral Reefs* 28(2):437–48

Correa AMS, Howard-Varona C, Coy SR, Buchan A, Sullivan MB, Weitz JS. 2021. Revisiting the rules of life for viruses of microorganisms. *Nat. Rev. Microbiol.* 19(8):501–13

Correa AMS, Welsh RM, Vega Thurber RL. 2013. Unique nucleocytoplasmic dsDNA and +ssRNA viruses are associated with the dinoflagellate endosymbionts of corals. *ISME J.* 7(1):13–27

Coy SR, Utama B, Spurlin JW, Kim JG, Deshmukh H, et al. 2023. Visualization of RNA virus infection in a marine protist with a universal biomarker. *Sci. Rep.* 13(1):5813

Croquer A, Weil E. 2009. Changes in Caribbean coral disease prevalence after the 2005 bleaching event. *Dis. Aquat. Organ.* 87(1–2):33–43

Davies SW, Gamache MH, Howe-Kerr LI, Kriefall NG, Baker AC, et al. 2023. Building consensus around the assessment and interpretation of Symbiodiniaceae diversity. *PeerJ* 11:e15023

Davy SK, Burchett SG, Dale AL, Davies P, Davy JE, et al. 2006. Viruses: agents of coral disease? *Dis. Aquat. Organ.* 69(1):101–10

Deutsch JM, Mandelare-Ruiz P, Yang Y, Foster G, Routhu A, et al. 2022. Metabolomics approaches to dereplicate natural products from coral-derived bioactive bacteria. *J. Nat. Prod.* 85(3):462–78

Dixon GB, Davies SW, Aglyamova GV, Meyer E, Bay LK, Matz MV. 2015. Genomic determinants of coral heat tolerance across latitudes. *Science* 348(6242):1460–62

Dobbelaere T, Muller EM, Gramer LJ, Holstein DM, Hanert E. 2020. Coupled epidemio-hydrodynamic modeling to understand the spread of a deadly coral disease in Florida. *Front. Mar. Sci.* 7:591881

Doering T, Wall M, Putchim L, Rattanawongwan T, Schroeder R, et al. 2021. Towards enhancing coral heat tolerance: a "microbiome transplantation" treatment using inoculations of homogenized coral tissues. *Microbiome* 9(1):102

Drappier M, Michiels T. 2015. Inhibition of the OAS/RNase L pathway by viruses. *Curr. Opin. Virol.* 15:19–26

Dustan P. 1977. Vitality of reef coral populations off Key Largo, Florida: recruitment and mortality. *Environ. Geol.* 2:51–58

Eaton KR, Clark AS, Curtis K, Favero M, Hanna Holloway N, et al. 2022. A highly effective therapeutic ointment for treating corals with black band disease. *PLOS ONE* 17(10):e0276902

Eddy TD, Cheung WWL, Bruno JF. 2018. Historical baselines of coral cover on tropical reefs as estimated by expert opinion. *PeerJ* 6:e4308

Efrony R, Atad I, Rosenberg E. 2009. Phage therapy of coral white plague disease: properties of phage BA3. *Curr. Microbiol.* 58(2):139–45

Epstein HE, Brown T, Akinrinade AO, McMinds R, Pollock FJ, et al. 2023. Evidence for microbially-mediated tradeoffs between growth and defense throughout coral evolution. bioRxiv 2023.04.26.538152. **https://doi.org/10.1101/2023.04.26.538152**

Foley JE, Sokolow SH, Girvetz E, Foley CW, Foley P. 2005. Spatial epidemiology of Caribbean yellow band syndrome in *Montastrea* spp. coral in the eastern Yucatan, Mexico. *Hydrobiologia* 548(1):33–40

Forrester GE, Arton L, Horton A, Nickles K, Forrester LM. 2022. Antibiotic treatment ameliorates the impact of stony coral tissue loss disease (SCTLD) on coral communities. *Front. Mar. Sci.* 9:859740

Francini-Filho RB, Moura RL, Thompson FL, Reis RM, Kaufman L, et al. 2008. Diseases leading to accelerated decline of reef corals in the largest South Atlantic reef complex (Abrolhos Bank, eastern Brazil). *Mar. Pollut. Bull.* 56(5):1008–14

Fraune S, Anton-Erxleben F, Augustin R, Franzenburg S, Knop M, et al. 2014. Bacteria-bacteria interactions within the microbiota of the ancestral metazoan Hydra contribute to fungal resistance. *ISME J.* 9(7):1543–56

Frias-Lopez J, Klaus JS, Bonheyo GT, Fouke BW. 2004. Bacterial community associated with black band disease in corals. *Appl. Environ. Microbiol.* 70(10):5955–62

Gignoux-Wolfsohn SA, Vollmer SV. 2015. Identification of candidate coral pathogens on white band disease-infected staghorn coral. *PLOS ONE* 10(8):e0134416

Gil-Agudelo DL, Smith GW, Weil E. 2006. The white band disease type II pathogen in Puerto Rico. *Rev. Biol. Trop.* 54:59–67

Goreau T, Cervino J, Goreau M, Hayes R, Hayes M, et al. 1998. Rapid spread of diseases in Caribbean coral reefs. *Rev. Biol. Trop.* 46:151–71

Gove JM, Williams GJ, Lecky J, Brown E, Conklin E, et al. 2023. Coral reefs benefit from reduced land-sea impacts under ocean warming. *Nature* 621(7979):536–42

Grasis JA. 2017. The intra-dependence of viruses and the holobiont. *Front. Immunol.* 8:1501

Griffin SP. 1998. The effects of sunlight on the progression of black band disease. *Rev. Biol. Trop.* 46:175–79

Grupstra CGB, Howe-Kerr LI, van der Meulen JA, Veglia AJ, Coy SR, Correa A. 2022a. Consumer feces impact coral health in guild-specific ways. *Front. Mar. Sci.* 10:1110346

Grupstra CGB, Howe-Kerr LI, Veglia AJ, Bryant RL, Coy SR, et al. 2022b. Thermal stress triggers productive viral infection of a key coral reef symbiont. *ISME J.* 16(5):1430–41

Heinz JM, Sommer M, Rosales SM, Lu J, Huebner LK, Salzberg SL. 2024. Novel metagenomics analysis suggests a species is associated with stony coral tissue loss disease. bioRxiv 2024.01.02.573916. **https://doi.org/10.1101/2024.01.02.573916**

Helgoe J, Davy SK, Weis VM, Rodriguez-Lanetty M. 2024. Triggers, cascades, and endpoints: connecting the dots of coral bleaching mechanisms. *Biol. Rev. Camb. Philos. Soc.* 99(3):715–52

Howe-Kerr LI, Grupstra CGB, Rabbitt KM, Conetta D, Coy SR, et al. 2023a. Viruses of a key coral symbiont exhibit temperature-driven productivity across a reefscape. *ISME Commun.* 3(1):27

Howe-Kerr LI, Knochel AM, Meyer MD, Sims JA, Karrick CE, et al. 2023b. Filamentous virus-like particles are present in coral dinoflagellates across genera and ocean basins. *ISME J.* 17(12):2389–402

Hudson JH. 2000. First aid for massive corals infected with black band disease, *Phormidium corallyticum*: an underwater aspirator and post-treatment sealant to curtail reinfection. In *Diving for Science in the 21st Century*, ed. P Hallock, L French, pp. 10–11. Nahant, MA: Am. Acad. Underw. Sci.

Jacquemot L, Bettarel Y, Monjol J, Corre E, Halary S, et al. 2018. Therapeutic potential of a new jumbo phage that infects *Vibrio coralliilyticus*, a widespread coral pathogen. *Front. Microbiol.* 9:2501

Jones RJ, Bowyer J, Hoegh-Guldberg O, Blackall LL. 2004. Dynamics of a temperature-related coral disease outbreak. *Mar. Ecol. Prog. Ser.* 281:63–77

Jutkina J, Marathe NP, Flach C-F, Larsson DGJ. 2018. Antibiotics and common antibacterial biocides stimulate horizontal transfer of resistance at low concentrations. *Sci. Total Environ.* 616–17:172–78

Kellogg CA, Piceno YM, Tom LM, DeSantis TZ, Gray MA, Andersen GL. 2014. Comparing bacterial community composition of healthy and dark spot-affected *Siderastrea siderea* in Florida and the Caribbean. *PLOS ONE* 9(10):e108767

Kiel PM, Formel N, Jankulak M, Baker A, Cunning R, et al. 2023. *Acropora cervicornis* Data Coordination Hub, an open access database for evaluating genet performance. *Bull. Mar. Sci.* 99(2):119–36

Kim HJ, Jun JW, Giri SS, Chi C, Yun S, et al. 2019. Application of the bacteriophage pVco-14 to prevent *Vibrio coralliilyticus* infection in Pacific oyster (*Crassostrea gigas*) larvae. *J. Invertebr. Pathol.* 167:107244

Kimes NE, Grim CJ, Johnson WR, Hasan NA, Tall BD, et al. 2011. Temperature regulation of virulence factors in the pathogen *Vibrio coralliilyticus*. *ISME J.* 6(4):835–46

Klein AM, Sturm AB, Eckert RJ, Walker BK, Neely KL, Voss JD. 2024. Algal symbiont genera but not coral host genotypes correlate to stony coral tissue loss disease susceptibility among *Orbicella faveolata* colonies in South Florida. *Front. Mar. Sci.* 11:1287457

Klepac CN, Petrik CG, Karabelas E, Owens J, Hall ER, Muller EM. 2024. Assessing acute thermal assays as a rapid screening tool for coral restoration. *Sci. Rep.* 14(1):1898

Kline DI, Vollmer SV. 2011. White band disease (type I) of endangered Caribbean acroporid corals is caused by pathogenic bacteria. *Sci. Rep.* 1(1):7

Klinges JG, Patel SH, Duke WC, Muller EM, Vega Thurber RL. 2022. Phosphate enrichment induces increased dominance of the parasite *Aquarickettsia* in the coral *Acropora cervicornis*. *FEMS Microbiol. Ecol.* 98(2):fiac013

Klinges JG, Patel SH, Duke WC, Muller EM, Vega Thurber RL. 2023. Microbiomes of a disease-resistant genotype of *Acropora cervicornis* are resistant to acute, but not chronic, nutrient enrichment. *Sci. Rep.* 13(1):3617

Koch HR, Azu Y, Bartels E, Muller EM. 2022a. No apparent cost of disease resistance on reproductive output in *Acropora cervicornis* genets used for active coral reef restoration in Florida. *Front. Mar. Sci.* 9:958500

Koch HR, Matthews B, Leto C, Engelsma C, Bartels E. 2022b. Assisted sexual reproduction of *Acropora cervicornis* for active restoration on Florida's Coral Reef. *Front. Mar. Sci.* 9:959520

Lawrence SA, Davy JE, Wilson WH, Hoegh-Guldberg O, Davy SK. 2015. *Porites* white patch syndrome: associated viruses and disease physiology. *Coral Reefs* 34(1):249–57

Lee Hing C, Guifarro Z, Dueñas D, Ochoa G, Nunez A, et al. 2022. Management responses in Belize and Honduras, as stony coral tissue loss disease expands its prevalence in the Mesoamerican reef. *Front. Mar. Sci.* 9:883062

Levin RA, Voolstra CR, Weynberg KD, van Oppen MJH. 2017. Evidence for a role of viruses in the thermal sensitivity of coral photosymbionts. *ISME J.* 11(3):808–12

Li J, Zou Y, Li Q, Zhang J, Bourne DG, et al. 2023. A coral-associated actinobacterium mitigates coral bleaching under heat stress. *Environ. Microbiome* 18(1):83

Littman R, Willis BL, Bourne DG. 2011. Metagenomic analysis of the coral holobiont during a natural bleaching event on the Great Barrier Reef. *Environ. Microbiol. Rep.* 3(6):651–60

MacKnight NJ, Cobleigh K, Lasseigne D, Chaves-Fonnegra A, Gutting A, et al. 2021. Microbial dysbiosis reflects disease resistance in diverse coral species. *Commun. Biol.* 4(1):679

MacKnight NJ, Dimos BA, Beavers KM, Muller EM, Brandt ME, Mydlarz LD. 2022. Disease resistance in coral is mediated by distinct adaptive and plastic gene expression profiles. *Sci. Adv.* 8(39):eabo6153

Malone TC, Newton A. 2020. The globalization of cultural eutrophication in the coastal ocean: causes and consequences. *Front. Mar. Sci*. 7:670

Mao-Jones J, Ritchie KB, Jones LE, Ellner SP. 2010. How microbial community composition regulates coral disease development. *PLOS Biol*. 8(3):e1000345

Marhaver KL, Edwards RA, Rohwer F. 2008. Viral communities associated with healthy and bleaching corals. *Environ. Microbiol.* 10(9):2277–86

Martinand C, Salehzada T, Silhol M, Lebleu B, Bisbal C. 1998. RNase L inhibitor (RLI) antisense constructions block partially the down regulation of the 2–5A/RNase L pathway in encephalomyocarditis-virus-(EMCV)-infected cells. *Eur. J. Biochem.* 254(2):248–55

Martínez-Castillo M, Pacheco-Yepez J, Flores-Huerta N, Guzmán-Téllez P, Jarillo-Luna RA, et al. 2018. Flavonoids as a natural treatment against *Entamoeba histolytica*. *Front. Cell. Infect. Microbiol.* 8:209

Martins BT, Correia da Silva M, Pinto M, Cidade H, Kijjoa A. 2019. Marine natural flavonoids: chemistry and biological activities. *Nat. Prod. Res.* 33(22):3260–72

Maynard J, van Hooidonk R, Eakin CM, Puotinen M, Garren M, et al. 2015. Projections of climate conditions that increase coral disease susceptibility and pathogen abundance and virulence. *Nat. Clim. Change* 5(7):688–94

Messyasz A, Rosales SM, Mueller RS, Sawyer T, Correa AMS, et al. 2020. Coral bleaching phenotypes associated with differential abundances of nucleocytoplasmic large DNA Viruses. *Front. Mar. Sci*. 7:555474

Meyer JL, Rodgers JM, Dillard BA, Paul VJ, Teplitski M. 2016. Epimicrobiota associated with the decay and recovery of *Orbicella* corals exhibiting dark spot syndrome. *Front. Microbiol.* 7:893

Miller AW, Richardson LL. 2011. A meta-analysis of 16S rRNA gene clone libraries from the polymicrobial black band disease of corals. *FEMS Microbiol. Ecol.* 75(2):231–41

Miller J, Muller EM, Rogers C, Waara R, Atkinson A, et al. 2009. Coral disease following massive bleaching in 2005 causes 60% decline in coral cover on reefs in the US Virgin Islands. *Coral Reefs* 28(4):925–37

Miller MW, Lohr KE, Cameron CM, Williams DE, Peters EC. 2014. Disease dynamics and potential mitigation among restored and wild staghorn coral, *Acropora cervicornis*. *PeerJ* 2:e541

Mohamed AR, Ochsenkühn MA, Kazlak AM, Moustafa A, Amin SA. 2023. The coral microbiome: towards an understanding of the molecular mechanisms of coral-microbiota interactions. *FEMS Microbiol. Rev.* 47(2):fuad005

Montalvo-Proaño J, Buerger P, Weynberg KD, van Oppen MJH. 2017. A PCR-based assay targeting the major capsid protein gene of a dinorna-like ssRNA virus that infects coral photosymbionts. *Front. Microbiol.* 8:1665

Morais J, Cardoso APLR, Santos BA. 2022. A global synthesis of the current knowledge on the taxonomic and geographic distribution of major coral diseases. *Environ. Adv.* 8:100231

Moriarty T, Leggat W, Huggett MJ, Ainsworth TD. 2020. Coral disease causes, consequences, and risk within coral restoration. *Trends Microbiol.* 28(10):793–807

Muller EM, Sartor C, Alcaraz NI, van Woesik R. 2020. Spatial epidemiology of the stony-coral-tissue-loss disease in Florida. *Front. Mar. Sci.* 7:163

Muller EM, van Woesik R. 2012. Caribbean coral diseases: primary transmission or secondary infection? *Glob. Change Biol.* 18(12):3529–35

Muller-Parker G, D'Elia CF, Cook CB. 2015. Interactions between corals and their symbiotic algae. In *Coral Reefs in the Anthropocene*, ed. C Birkeland, pp. 99–116. Dordrecht, Neth.: Springer

Mydlarz LD, Couch CS, Weil E, Smith G, Harvell CD. 2009. Immune defenses of healthy, bleached and diseased *Montastraea faveolata* during a natural bleaching event. *Dis. Aquat. Organ.* 87(1–2):67–78

Mydlarz LD, Muller EM. 2023. Genetics of coral resilience. *Science* 381(6665):1414–15

NASEM (Natl. Acad. Sci. Eng. Med.). 2019. *A Research Review of Interventions to Increase the Persistence and Resilience of Coral Reefs*. Washington, DC: Natl. Acad. Press

Neely KL, Shea CP, Macaulay KA, Hower EK, Dobler MA. 2021. Short- and long-term effectiveness of coral disease treatments. *Front. Mar. Sci.* 8:675349

Nguyen-Kim H, Bettarel Y, Bouvier T, Bouvier C, Doan-Nhu H, et al. 2015. Coral mucus is a hot spot for viral infections. *Appl. Environ. Microbiol.* 81(17):5773–83

Nielsen DA, Petrou K, Gates RD. 2018. Coral bleaching from a single cell perspective. *ISME J.* 12(6):1558–67

Oechslin F. 2018. Resistance development to bacteriophages occurring during bacteriophage therapy. *Viruses* 10(7):351

Page CA, Croquer A, Bastidas C, Rodríguez S, Neale SJ, et al. 2015. *Halofolliculina* ciliate infections on corals (skeletal eroding disease). In *Diseases of Coral*, ed. CM Woodley, CA Downs, AW Bruckner, JW Porter, SB Galloway, pp. 361–75. Hoboken, NJ: Wiley & Sons

Page CA, Willis BL. 2008. Epidemiology of skeletal eroding band on the Great Barrier Reef and the role of injury in the initiation of this widespread coral disease. *Coral Reefs* 27(2):257–72

Page CE, Leggat W, Egan S, Ainsworth TD. 2023. A coral disease outbreak highlights vulnerability of remote high-latitude lagoons to global and local stressors. *iScience* 26(3):106205

Palmer CV, Bythell JC, Willis BL. 2010. Levels of immunity parameters underpin bleaching and disease susceptibility of reef corals. *FASEB J.* 24(6):1935–46

Palmer CV, Gates RD. 2010. Skeletal eroding band in Hawaiian corals. *Coral Reefs* 29(2):469

Papke E, Carreiro A, Dennison C, Deutsch JM, Isma LM, et al. 2024. Stony coral tissue loss disease: a review of emergence, impacts, etiology, diagnostics, and intervention. *Front. Mar. Sci.* 10:1321271

Peixoto RS, Rosado PM, Leite DCA, Rosado AS, Bourne DG. 2017. Beneficial microorganisms for corals (BMC): proposed mechanisms for coral health and resilience. *Front. Microbiol.* 8:341

Peixoto RS, Sweet M, Villela HDM, Cardoso P, Thomas T, et al. 2021. Coral probiotics: premise, promise, prospects. *Annu. Rev. Anim. Biosci.* 9:265–88

Pinzón JH, Kamel B, Burge CA, Harvell CD, Medina M, et al. 2015. Whole transcriptome analysis reveals changes in expression of immune-related genes during and after bleaching in a reef-building coral. *R. Soc. Open Sci.* 2(4):140214

Pogoreutz C, Ziegler M. 2023. Frenemies on the reef? Resolving the coral–*Endozoicomonas* association. *Trends Microbiol.* 32(5):422–34

Pollock FJ, Lamb JB, van de Water JAJM, Smith HA, Schaffelke B, et al. 2019. Reduced diversity and stability of coral-associated bacterial communities and suppressed immune function precedes disease onset in corals. *R. Soc. Open Sci.* 6(6):190355

Quistad SD, Grasis JA, Barr JJ, Rohwer FL. 2017. Viruses and the origin of microbiome selection and immunity. *ISME J.* 11(4):835–40

Rädecker N, Escrig S, Spangenberg JE, Voolstra CR, Meibom A. 2023. Coupled carbon and nitrogen cycling regulates the cnidarian-algal symbiosis. *Nat. Commun.* 14(1):6948

Randall CJ, van Woesik R. 2015. Contemporary white-band disease in Caribbean corals driven by climate change. *Nat. Clim. Change* 5(4):375–79

Randall CJ, Whitcher EM, Code T, Pollock C, Lundgren I, et al. 2018. Testing methods to mitigate Caribbean yellow-band disease on *Orbicella faveolata*. *PeerJ* 6:e4800

Raymundo LJ. 2008. *Coral Disease Handbook: Guidelines for Assessment, Monitoring and Management*. St. Lucia, Aust.: Coral Reef Target. Res. Capacity Build. Manag. Program

Reeves L. 1994. Newly discovered: yellow band disease strikes keys reefs. *Underw. USA* 11(8):16

Reshef L, Koren O, Loya Y, Rosenberg I, Rosenberg E. 2006. The coral probiotic hypothesis. *Environ. Microbiol.* 8(12):2068–73

Ricci F, Leggat W, Page CE, Ainsworth TD. 2022. Coral growth anomalies, neoplasms, and tumors in the Anthropocene. *Trends Microbiol.* 30(12):1160–73

Rich LP, Arnot C, Dennis MM. 2021. Pathology of growth anomalies in massive Caribbean corals of the family Faviidae. *Vet. Pathol.* 58(6):1119–30

Richardson LL. 1996. Horizontal and vertical migration patterns of *Phormidium corallyticum* and *Beggiatoa* spp. associated with black-band disease of corals. *Microb. Ecol.* 32(3):323–35

Richardson LL. 1998. Coral diseases: What is really known? *Trends Ecol. Evol.* 13(11):438–43

Richardson LL. 2012. Arnfried Antonius, coral diseases, and the AMLC. *Rev. Biol. Trop.* 60:13–20

Richardson LL, Kuta KG. 2003. Ecological physiology of the black band disease cyanobacterium *Phormidium corallyticum*. *FEMS Microbiol. Ecol.* 43(3):287–98

Ritchie KB, Smith GW. 1998. Type II white-band disease. *Rev. Biol. Trop.* 46:199–203

Roberts JA, Kruger P, Paterson DL, Lipman J. 2008. Antibiotic resistance—what's dosing got to do with it? *Crit. Care Med.* 36(8):2433–40

Rosado PM, Leite DCA, Duarte GAS, Chaloub RM, Jospin G, et al. 2019. Marine probiotics: increasing coral resistance to bleaching through microbiome manipulation. *ISME J.* 13(4):921–36

Rosales SM, Huebner LK, Clark AS, McMinds R, Ruzicka RR, Muller EM. 2022. Bacterial metabolic potential and micro-eukaryotes enriched in stony coral tissue loss disease lesions. *Front. Mar. Sci.* 8:776859

Rosales SM, Huebner LK, Evans JS, Apprill A, Baker AC, et al. 2023. A meta-analysis of the stony coral tissue loss disease microbiome finds key bacteria in unaffected and lesion tissue in diseased colonies. *ISME Commun.* 3(1):19

Rosenberg E, Loya Y, eds. 2004. *Coral Health and Disease*. Berlin: Springer

Rouzé H, Lecellier G, Saulnier D, Berteaux-Lecellier V. 2016. *Symbiodinium* clades A and D differentially predispose *Acropora cytherea* to disease and *Vibrio* spp. colonization. *Ecol. Evol.* 6(2):560–72

Rubio-Portillo E, Yarza P, Peñalver C, Ramos-Esplá AA, Antón J. 2014. New insights into *Oculinapatagonica* coral diseases and their associated *Vibrio* spp. communities. *ISME J.* 8(9):1794–807

Rutzler K, Santavy DL, Antonius A. 1983. The black band disease of Atlantic reef corals. *Mar. Ecol.* 4(4):329–58

Sachs JL, Wilcox TP. 2006. A shift to parasitism in the jellyfish symbiont *Symbiodinium microadriaticum*. *Proc. R. Soc. B* 273(1585):425–29

Santoro EP, Borges RM, Espinoza JL, Freire M, Messias CSMA, et al. 2021. Coral microbiome manipulation elicits metabolic and genetic restructuring to mitigate heat stress and evade mortality. *Sci. Adv.* 7(33):eabg3088

Seveso D, Montano S, Reggente MA, Orlandi I, Galli P, Vai M. 2015. Modulation of Hsp60 in response to coral brown band disease. *Dis. Aquat. Organ.* 115(1):15–23

Shilling EN, Combs IR, Voss JD. 2021. Assessing the effectiveness of two intervention methods for stony coral tissue loss disease on *Montastraea cavernosa*. *Sci. Rep.* 11(1):8566

Silva-Lima AW, Froes AM, Garcia GD, Tonon LAC, Swings J, et al. 2021. *Mussismilia braziliensis* white plague disease is characterized by an affected coral immune system and dysbiosis. *Microb. Ecol.* 81(3):795–806

Silverstein RN, Correa AMS, Baker AC. 2012. Specificity is rarely absolute in coral-algal symbiosis: implications for coral response to climate change. *Proc. R. Soc. B* 279(1738):2609–18

Soffer N, Brandt ME, Correa AMS, Smith TB, Thurber RV. 2013. Potential role of viruses in white plague coral disease. *ISME J.* 8(2):271–83

Solano OD, Navas Suarez G, Moreno-Forero SK. 1993. Blanqueamiento coralino de 1990 en el Parque Nacional Natural Corales del Rosario (Caribe, colombiano). *Bol. Investig. Mar. Costeras* 22(1):97–111

Spies NP, Takabayashi M. 2013. Expression of galaxin and oncogene homologs in growth anomaly in the coral *Montipora capitata*. *Dis. Aquat. Organ.* 104(3):249–56

Studivan MS, Eckert RJ, Shilling E, Soderberg N, Enochs IC, Voss JD. 2023. Stony coral tissue loss disease intervention with amoxicillin leads to a reversal of disease-modulated gene expression pathways. *Mol. Ecol.* 32(19):5394–5413

Sutherland KP, Porter JW, Torres C. 2004. Disease and immunity in Caribbean and Indo-Pacific zooxanthellate corals. *Mar. Ecol. Prog. Ser.* 266:273–302

Sweet M, Andradi-Brown DA, Voolstra CR, Head CEI, Curnick D, et al., eds. 2020. *Coral Reefs in the Anthropocene*. Lausanne, Switz.: Front. Media

Sweet M, Burn D, Croquer A, Leary P. 2013a. Characterisation of the bacterial and fungal communities associated with different lesion sizes of dark spot syndrome occurring in the coral *Stephanocoenia intersepta*. *PLOS ONE* 8(4):e62580

Sweet M, Bythell JC. 2012. Ciliate and bacterial communities associated with white syndrome and brown band disease in reef-building corals. *Environ. Microbiol.* 14(8):2184–99

Sweet M, Bythell JC, Nugues MM. 2013b. Algae as reservoirs for coral pathogens. *PLOS ONE* 8(7):e69717

Sweet M, Croquer A, Bythell JC. 2014. Experimental antibiotic treatment identifies potential pathogens of white band disease in the endangered Caribbean coral *Acropora cervicornis*. *Proc. R. Soc. B* 281(1788):20140094

Sweet M, Villela H, Keller-Costa T, Costa R, Romano S, et al. 2021. Insights into the cultured bacterial fraction of corals. *mSystems* 6(3):01249-20

Tavares-Carreon F, De Anda-Mora K, Rojas-Barrera IC, Andrade A. 2023. *Serratia marcescens* antibiotic resistance mechanisms of an opportunistic pathogen: a literature review. *PeerJ* 11:e14399

Thompson FL, Barash Y, Sawabe T, Sharon G, Swings J, Rosenberg E. 2006. *Thalassomonas loyana* sp. nov., a causative agent of the white plague-like disease of corals on the Eilat coral reef. *Int. J. Syst. Evol. Microbiol.* 56(2):365–68

Toller WW, Rowan R, Knowlton N. 2001. Zooxanthellae of the *Montastraea annularis* species complex: patterns of distribution of four taxa of *Symbiodinium* on different reefs and across depths. *Biol. Bull.* 201(3):348–59

Tomaru Y, Katanozaka N, Nishida K, Shirai Y, Tarutani K, et al. 2004. Isolation and characterization of two distinct types of HcRNAV, a single-stranded RNA virus infecting the bivalve-killing microalga *Heterocapsa circularisquama*. *Aquat. Microb. Ecol.* 34:207–18

Tomaru Y, Mizumoto H, Nagasaki K. 2009. Virus resistance in the toxic bloom-forming dinoflagellate *Heterocapsa circularisquama* to single-stranded RNA virus infection. *Environ. Microbiol.* 11(11):2915–23

Ulstrup KE, Kühl M, Bourne DG. 2007. Zooxanthellae harvested by ciliates associated with brown band syndrome of corals remain photosynthetically competent. *Appl. Environ. Microbiol.* 73(6):1968–75

Ushijima B, Gunasekera SP, Meyer JL, Tittl J, Pitts KA, et al. 2023. Chemical and genomic characterization of a potential probiotic treatment for stony coral tissue loss disease. *Commun. Biol.* 6(1):248

van Oppen MJH, Leong J-A, Gates RD. 2009. Coral-virus interactions: a double-edged sword? *Symbiosis* 47(1):1–8

van Woesik R, Randall CJ. 2017. Coral disease hotspots in the Caribbean. *Ecosphere* 8(5):e01814

Vega Thurber RL, Barott KL, Hall D, Liu H, Rodriguez-Mueller B, et al. 2008. Metagenomic analysis indicates that stressors induce production of herpes-like viruses in the coral *Porites compressa*. *PNAS* 105(47):18413–18

Vega Thurber RL, Burkepile DE, Fuchs C, Shantz AA, McMinds R, Zaneveld JR. 2014. Chronic nutrient enrichment increases prevalence and severity of coral disease and bleaching. *Glob. Change Biol.* 20(2):544–54

Vega Thurber RL, Correa AMS. 2023. *Meta-transcriptomics to determine if and how viruses are involved in SCTLD infection status and/or disease susceptibility*. Rep., Fla. Dep. Environ. Prot., Miami

Vega Thurber RL, Mydlarz LD, Brandt M, Harvell CD, Weil E, et al. 2020. Deciphering coral disease dynamics: integrating host, microbiome, and the changing environment. *Front. Ecol. Evol.* 8:575927

Vega Thurber RL, Payet JP, Thurber AR, Correa AMS. 2017. Virus-host interactions and their roles in coral reef health and disease. *Nat. Rev. Microbiol.* 15(4):205–16

Vega Thurber RL, Willner-Hall D, Rodriguez-Mueller B, Desnues C, Edwards RA, et al. 2009. Metagenomic analysis of stressed coral holobionts. *Environ. Microbiol.* 11(8):2148–63

Veglia AJ. 2023. *Detecting and interpreting viral dynamics in marine invertebrate holobionts*. PhD Thesis, Rice Univ., Houston, TX

Veglia AJ, Beavers K, Van Buren EW, Meiling SS, Muller EM, et al. 2022. Alphaflexivirus genomes in stony coral tissue loss disease-affected, disease-exposed, and disease-unexposed coral colonies in the U.S. Virgin Islands. *Microbiol. Resour. Announc.* 11(2):e0119921

Veglia AJ, Bistolas KSI, Voolstra CR, Hume BCC, Ruscheweyh H-J, et al. 2023. Endogenous viral elements reveal associations between a non-retroviral RNA virus and symbiotic dinoflagellate genomes. *Commun. Biol.* 6(1):566

Veglia AJ, Milford CR, Schizas NV. 2021. Isolation and genotyping of novel T4 cyanophages associated with diverse coral reef invertebrates. *Coral Reefs* 40(2):485–504

Veglia AJ, Rivera-Vicéns RE, Grupstra CGB, Howe-Kerr LI, Correa AMS. 2024. vAMPirus: a versatile amplicon processing and analysis program for studying viruses. *Mol. Ecol. Resour.* 24(6):e13978

Viehman S, Mills DK, Meichel GW, Richardson LL. 2006. Culture and identification of *Desulfovibrio* spp. from corals infected by black band disease on Dominican and Florida Keys reefs. *Dis. Aquat. Organ.* 69(1):119–27

Vollmer SV, Selwyn JD, Despard BA, Roesel CL. 2023. Genomic signatures of disease resistance in endangered staghorn corals. *Science* 381(6665):1451–54

Vompe AD, Epstein HE, Speare KE, Schmeltzer ER, Adam TC, et al. 2024. Microbiome ecological memory and responses to repeated marine heatwaves clarify variation in coral bleaching and mortality. *Glob. Change Biol.* 30(1):e17088

Voolstra CR, Raina J-B, Dörr M, Cárdenas A, Pogoreutz C, et al. 2024. The coral microbiome in sickness, in health and in a changing world. *Nat. Rev. Microbiol.* 22(8):460–76

Voolstra CR, Suggett DJ, Peixoto RS, Parkinson JE, Quigley KM, et al. 2021. Extending the natural adaptive capacity of coral holobionts. *Nat. Rev. Earth Environ.* 2(11):747–62

Voss JD, Richardson LL. 2006. Nutrient enrichment enhances black band disease progression in corals. *Coral Reefs* 25(4):569–76

Walker BK, Turner NR, Noren HKG, Buckley SF, Pitts KA. 2021. Optimizing stony coral tissue loss disease (SCTLD) intervention treatments on *Montastraea cavernosa* in an endemic zone. *Front. Mar. Sci.* 8:666224

Wang L, Shantz AA, Payet JP, Sharpton T, Foster A, et al. 2018. Corals and their microbiomes are differentially affected by exposure to elevated nutrients and a natural thermal anomaly. *Front. Mar. Sci.* 5:101

Ward JR. 2006. *Ecology of marine diseases: coral reef community diversity, host resistance, and climate change*. PhD Thesis, Cornell Univ., Ithaca, NY

Weil E, Croquer A, Urreiztieta I. 2009a. Temporal variability and impact of coral diseases and bleaching in La Parguera, Puerto Rico from 2003–2007. *Caribb. J. Sci.* 45(2–3):221–46

Weil E, Croquer A, Urreiztieta I. 2009b. Yellow band disease compromises the reproductive output of the Caribbean reef-building coral *Montastraea faveolata* (Anthozoa, Scleractinia). *Dis. Aquat. Organ.* 87(1–2):45–55

Welsh RM, Rosales SM, Zaneveld JR, Payet JP, McMinds R, et al. 2017. Alien vs. predator: bacterial challenge alters coral microbiomes unless controlled by *Halobacteriovorax* predators. *PeerJ* 5:e3315

Welsh RM, Zaneveld JR, Rosales SM, Payet JP, Burkepile DE, Thurber RV. 2016. Bacterial predation in a marine host-associated microbiome. *ISME J.* 10(6):1540–44

Weynberg KD, Laffy PW, Wood-Charlson EM, Turaev D, Rattei T, et al. 2017a. Coral-associated viral communities show high levels of diversity and host auxiliary functions. *PeerJ* 5:e4054

Weynberg KD, Neave M, Clode PL, Voolstra CR, Brownlee C, et al. 2017b. Prevalent and persistent viral infection in cultures of the coral algal endosymbiont *Symbiodinium*. *Coral Reefs* 36(3):773–84

Weynberg KD, Wood-Charlson EM, Suttle CA, van Oppen MJH. 2014. Generating viral metagenomes from the coral holobiont. *Front. Microbiol.* 5:206

Wiedenmann J, D'Angelo C, Mardones ML, Moore S, Benkwitt CE, et al. 2023. Reef-building corals farm and feed on their photosynthetic symbionts. *Nature* 620(7976):1018–24

Williams SD, Walter CS, Muller EM. 2021. Fine scale temporal and spatial dynamics of the stony coral tissue loss disease outbreak within the lower Florida Keys. *Front. Mar. Sci.* 8:631776

Willis BL, Page CA, Dinsdale EA. 2004. Coral disease on the Great Barrier Reef. In *Coral Health and Disease*, ed. E Rosenberg, Y Loya, pp. 69–104. Berlin: Springer

Wilson WH, Francis I, Ryan K, Davy S. 2001. Temperature induction of viruses in symbiotic dinoflagellates. *Aquat. Microb. Ecol.* 25:99–102

Winkler R, Antonius A, Renegar DA. 2004. The skeleton eroding band disease on coral reefs of Aqaba, Red Sea. *Mar. Ecol.* 25(2):129–44

Wood-Charlson EM, Weynberg KD, Suttle CA, Roux S, van Oppen MJH. 2015. Metagenomic characterization of viral communities in corals: mining biological signal from methodological noise. *Environ. Microbiol.* 17(10):3440–49

Woodley CM, Downs CA, Bruckner AW, Porter JW, Galloway SB, eds. 2015. *Diseases of Coral*. Hoboken, NJ: Wiley & Sons

Work TM, Aeby GS. 2006. Systematically describing gross lesions in corals. *Dis. Aquat. Org.* 70(1–2):155–60

Work TM, Meteyer C. 2014. To understand coral disease, look at coral cells. *EcoHealth* 11(4):610–18

Work TM, Weatherby TM, Landsberg JH, Kiryu Y, Cook SM, Peters EC. 2021. Viral-like particles are associated with endosymbiont pathology in Florida corals affected by stony coral tissue loss disease. *Front. Mar. Sci.* 8:750658

Zhang Y, Yang Q, Ling J, Long L, Huang H, et al. 2021. Shifting the microbiome of a coral holobiont and improving host physiology by inoculation with a potentially beneficial bacterial consortium. *BMC Microbiol.* 21(1):130

Zvuloni A, Artzy-Randrup Y, Stone L, Kramarsky-Winter E, Barkan R, Loya Y. 2009. Spatio-temporal transmission patterns of black-band disease in a coral community. *PLOS ONE* 4(4):e4993