



Extending the natural adaptive capacity of coral holobionts

Item Type	Article
Authors	Voolstra, Christian R.;Suggett, David J.;Peixoto, Raquel S.;Parkinson, John E.;Quigley, Kate M.;Silveira, Cynthia B.;Sweet, Michael;Muller, Erinn M.;Barshis, Daniel J.;Bourne, David G.;Aranda, Manuel
Citation	Voolstra, C. R., Suggett, D. J., Peixoto, R. S., Parkinson, J. E., Quigley, K. M., Silveira, C. B., ... Aranda, M. (2021). Extending the natural adaptive capacity of coral holobionts. Nature Reviews Earth & Environment. doi:10.1038/s43017-021-00214-3
Eprint version	Post-print
DOI	10.1038/s43017-021-00214-3
Publisher	Springer Science and Business Media LLC
Journal	Nature Reviews Earth & Environment
Rights	Archived with thanks to Nature Reviews Earth & Environment
Download date	2024-04-12 15:04:14
Link to Item	http://hdl.handle.net/10754/672818

Extending the natural adaptive capacity of coral holobionts

Christian R. Voolstra^{1, †}, David J. Suggett², Raquel Peixoto^{3,4}, John E. Parkinson⁵, Kate M. Quigley⁶, Cynthia B. Silveira⁷, Michael Sweet⁸, Erinn M. Muller⁹, Daniel J. Barshis¹⁰, David G. Bourne^{6,11} and Manuel Aranda³

¹ Department of Biology, University of Konstanz, Konstanz, Germany

² Climate Change Cluster, Faculty of Science, University of Technology Sydney, Ultimo, NSW, Australia

³ Red Sea Research Center (RSRC), Division of Biological and Environmental Science and Engineering (BESE), King Abdullah University of Science and Technology (KAUST), Saudi Arabia

⁴ Institute of Microbiology, Federal University of Rio de Janeiro (UFRJ), Rio de Janeiro, Brazil

⁵ Department of Integrative Biology, University of South Florida, Tampa, FL, USA

⁶ Australian Institute of Marine Science, Townsville, QLD, Australia

⁷ Department of Biology, University of Miami, Coral Gables, FL, USA

⁸ Aquatic Research Facility, Environmental Sustainability Research Centre, University of Derby, Derby, UK

⁹ Mote Marine Laboratory, Sarasota, FL, USA

¹⁰ Department of Biological Sciences, Old Dominion University, Norfolk, VA, USA

¹¹ College of Science and Engineering, James Cook University, Townsville, QLD, Australia

† email: christian.voolstra@uni-konstanz.de

Abstract

Anthropogenic climate change and environmental degradation destroy coral reefs, the ecosystem services they provide, and the livelihoods of close to a billion people who depend on these services. Restoration approaches to increase the resilience of corals are therefore necessary to counter environmental pressures relevant to climate change projections. In this Review, we examine the natural processes that can increase the adaptive capacity of coral holobionts, with the aim of preserving ecosystem functioning under future ocean conditions. Current approaches that center around restoring reef cover can be integrated with emerging approaches to enhance coral stress resilience and thereby allow reefs to regrow under a new set of environmental conditions. Emerging approaches, such as standardized acute thermal stress assays, selective sexual propagation, coral probiotics and environmental hardening could be feasible and scalable in the real world. However, they must follow decision-making criteria that consider the different reef, environmental and ecological conditions. The implementation of adaptive interventions tailored around nature-based solutions will require standardized frameworks, appropriate ecological risk-benefit assessments, and analytical routines for consistent and effective utilization and global coordination.

41 [H1] Introduction

42 Tropical coral reefs cover only 0.1% of the seafloor yet provide habitat for >30% of all marine
43 multicellular species¹. Ecosystem services delivered through healthy tropical reefs are
44 economically valued at around 9.9 trillion USD per year² and sustain almost a billion people³⁻⁵.
45 Despite their importance, catastrophic global loss of coral reefs owing to anthropogenic activity is
46 fast becoming a reality⁶. For example, the 2015-2018 global coral bleaching [G] event affected
47 74% of worldwide reefs, with >30% of coral cover lost on the Great Barrier Reef alone⁷.
48 Additionally, coral cover in the Florida Reef Tract (has declined by upwards of 90% over the last
49 50 years⁸⁻¹¹.

50
51 A global contributing factor to reef degradation is coral bleaching^{12,13}. Without their microalgal
52 symbionts (**Fig. 1**), corals lose their primary source of nutrition, leading to starvation, reduced
53 fecundity and growth, often resulting in widespread coral mortality^{14,15}. Trajectories for coral reefs
54 under present CO₂ emission scenarios are dire, with 60% of all remaining coral reefs critically
55 threatened, and 98% exposed to environmental conditions above current thresholds considered
56 necessary to maintain ecosystem function as soon as 2030 (ref¹⁶). The impact of ocean warming
57 is exacerbated by the effects of ocean acidification¹⁷, deoxygenation¹⁸ and salinity changes¹⁹.
58 Combined with local factors such as overfishing, coastal development, disturbance of the nutrient
59 environment (water quality) and disease or predator outbreaks, the interrelated cumulative
60 impacts all contribute to reduction in coral cover and declining reef ecosystem health²⁰⁻²⁷.

61
62 Given the rate and extent at which climate change unfolds²⁸, a widespread and shared concern
63 is that the rate of environmental change could outpace the ability of coral holobionts to adapt to
64 the changing environment²⁹, concomitant with the increasing loss of coral reef cover³⁰. Global
65 mitigation of CO₂ emissions is unquestionably needed to stem the rate of declining reef health
66^{30,31}. However, biological, ecological and socio-economic adaptations are critical partners to
67 preserve reefs and delay the loss of coral populations until carbon mitigation is effectively
68 implemented³⁰. Reef protection through Marine Protected Areas and management practices
69 reduces how local stressors compound global climate change impacts^{27,31}. Nevertheless, the
70 current status of reefs and their predicted further decline has sparked initiatives to prioritize reefs
71 or corals that are less vulnerable to climate change and best positioned for regenerating other
72 degraded reefs in the future³²⁻³⁴.

73
74 An active area of investigation is the development of intervention management tools to maintain
75 or even rebuild reefs, enhance recovery rates and promote resistance to environmental pressures
76 through ecological engineering, assisted evolution [G], and managed relocation³⁵⁻³⁹. Success of
77 any of these initiatives requires detailed knowledge on the long-term survivability of reefs, which,
78 in turn, relies on better understanding the biotic and abiotic factors that underlie coral stress
79 tolerance and the identification of colonies with such characteristics⁴⁰⁻⁴². Projecting further, active
80 manipulation of the natural adaptive capacity [G] of coral holobionts might be needed to reverse
81 the trend of ongoing reef loss.

82
83 Understanding how corals function is fundamental to the success of any approach that exploits
84 or manipulates their natural capacity to adapt⁴³⁻⁴⁵. Consequently, all the entities that constitute

85 the coral holobiont (**Fig. 1**) must be considered. Given the vastly different biologies of sessile
86 coral animals, their eukaryotic microalgae, prokaryotes (bacteria and archaea) and viruses
87 (amongst others), the adaptive responses operate on different time scales and are subject to
88 unique evolutionary and ecological contexts of adaptation ^{44,46}. Knowledge about how coral
89 holobionts respond or adapt to stressors provides the opportunity to modify these responses,
90 employing or manipulating the same mechanisms that corals have naturally evolved to survive
91 stress. Although knowledge of how corals adapt to environmental stress is limited, emerging
92 information on the biological entities that constitute the coral holobiont (and improved methods to
93 manipulate them) provides opportunities to harness their individual and collective natural adaptive
94 responses ^{35,40,47–53}.

95
96 In this Review, we describe an adaptive intervention framework aimed at harnessing the natural
97 adaptive capacity of the coral holobiont. Expanding the adaptive capacity relies on
98 operationalizing nascent methodological innovations at scale and is dependent on making them
99 cost-effective, risk-reward favorable and tailored to the challenges faced by the specific
100 environmental conditions of different reefs. The adaptive strategies available to the different coral
101 holobiont entities and how the underlying mechanisms might be employed or manipulated to
102 increase stress resilience at large are summarized with a focus on thermal tolerance.
103 Subsequently, a blueprint for coral survival guided by scientific insight utilizing emerging methods
104 and technologies and how they can be implemented and scaled to real world application is
105 outlined, emphasizing that feasibility needs to be weighed against scalability, practicality, and
106 regional setting to provide tailored and scaled solutions.
107

108 **[H1] Adaptive Strategies of Coral Hosts**

109 Like all animals, corals respond to changes in their environment via **acclimation [G]** and
110 adaptation. Adaptation does not *sensu stricto* refer to evolutionary change through positive
111 selection but is more broadly used to denote adjusting to prevailing environmental conditions by
112 various means ⁴⁴. Here, the term **environmental adaptation [G]** is used in this broad sense and
113 **evolutionary adaptation [G]** denotes the specific process of natural selection.

114
115 The extent to which corals can acclimate to alleviate environmental stress is currently unclear,
116 although some corals do appear to demonstrate a large capacity for acclimation. For example,
117 colonies (genotypes) of some species can survive for hundreds if not thousands of years while
118 experiencing dramatic environmental changes during their lifetime ^{54,55}. In American Samoa,
119 *Acropora hyacinthus* coral fragments that were transplanted between adjacent pools with different
120 thermal environments demonstrated acquisition of heat tolerance levels by means of acclimation
121 that would be expected from adaptation through natural selection over multiple generations ⁵⁶.
122 Naturally heat-resistant coral transplants in Hawaii acclimated to new environmental regimes on
123 the scale of months, maintaining the corals' heat stress response ⁵⁷.

124
125 Notably, acclimation capacity differs amongst coral species and appears inherently linked to the
126 ability to mount rapid and lasting widespread transcriptomic changes ^{58–61} or reprogramming

127 epigenetic marks^{62–64}. In addition to acclimation within the lifetime of an animal, transgenerational
128 plasticity might enable corals to acclimate to prevailing environmental conditions⁴⁶. Such
129 acclimation has been observed in experiments comparing the performance of offspring from
130 parents raised in different environments where acquired tolerances are passed on to the next
131 generation^{65–67}, potentially linking transgenerational acclimation to DNA methylation⁴⁹.

132
133 Evolutionary adaptation through natural selection usually requires multiple generations, as the
134 prevalence of selected alleles underlying the beneficial trait needs to increase and become a
135 common trait of the population or species. Therefore, this process depends on several variables,
136 such as the amount of genetic variation present in the population, the population size, generation
137 time and the strength of selection. The standing genetic diversity of corals is presumably large^{68–}
138 ⁷⁰, suggesting a capacity to recover from reductions in population size under suitable conditions,
139 at least for some species⁷⁰. Corals could also have the capacity to adapt via heritable somatic
140 mutations^{71,72}. The ability to adapt rapidly (years to decades) to changing environments is further
141 supported by the presence and frequency of thermotolerance alleles and the modelling of
142 population trajectories under different climate change scenarios^{69,73}. Indeed, natural populations
143 might already be adapting to increasing sea surface temperatures^{74–76} or have previously adapted
144 to extreme environmental conditions^{77–79}.

145
146 The ability of at least some coral species to exhibit substantial acclimation capacity presents the
147 possibility to harness this capacity for reef **restoration [G]** through a process termed
148 **environmental hardening [G]** (**Table 1**). For example, pre-conditioned coral fragments show
149 increased resilience compared with naive coral fragments in some species^{59,80}. These effects
150 might even be passed on to the next generation^{65–67,81}. Although the molecular mechanisms
151 underlying these effects are not yet fully understood, epigenetic modifications, such as DNA
152 methylation and histone modification, amongst others, might be involved⁴⁶. DNA methylation
153 changes have been found in response to stress treatments⁶² or transplantation⁸², and were not
154 only predictive of phenotypic responses, but also showed higher correlation than changes in gene
155 expression. More importantly, corals (in contrast to other metazoans) appear to biparentally pass
156 on their DNA methylation patterns to their offspring, thereby providing a molecular mechanism for
157 transgenerational inheritance of acclimation responses⁴⁹. If such mechanisms indeed exist, they
158 could be exploited by growing corals in land-based nurseries that allow controlled exposure to
159 increased temperature or other stressors to induce favorable acclimation responses⁸³.

160
161 The extent to which resilience can be improved through environmental hardening and
162 transgenerational acclimation is unclear. For example, there is still little understanding of which
163 mechanisms promote this effect, the extent that resilience can be increased, or how long the
164 preconditioning effects are maintained. By comparison, assessments on the potential of selective
165 breeding as a means to achieve coral adaptation have provided promising insights to improve
166 restoration approaches through human intervention. Similarly, breeding experiments reveal that
167 genetic adaptations to higher temperatures can be passed on within a single generation, with
168 coral larvae from parents of warmer regions producing offspring with up to 10 times higher
169 chances of survival under heat stress⁸⁴. Importantly, the survival odds still increased by up to

170 five-fold if only one of the parents came from a warmer region, providing evidence for the
171 increasing thermotolerance of corals via assisted evolution ³⁵.

172

173 Assisted evolution interventions follow the premise that “nature does it best”. Such approaches
174 are generally less extreme than targeted genetic modification approaches; they rely on naturally
175 occurring genotypes and natural selection to counter any drastic genetic alterations that would
176 affect the remainder of the coral holobiont and its genetic constituents. Several interventions are
177 proposed, such as the relocation of thermotolerant colonies (genotypes) to cooler regions to
178 introduce adaptive genetic variants into these populations or selective breeding using
179 thermotolerant colonies ^{35,38,85}. Both methods attempt to mimic natural processes by increasing
180 the frequency of beneficial alleles in the local population, providing a foundation for selection,
181 while retaining both genetic diversity and the local genetic adaptations required for the success
182 of corals at the specific location. Importantly, both methods rely on the identification and selection
183 of thermotolerant genotypes (such as those from particularly warmer environments, like lagoonal
184 pools). This identification requires the development of large-scale phenotyping platforms and
185 knowledge of the natural distribution range of coral species under study. Selecting more stress
186 tolerant and resilient genotypes is a non-trivial task given the challenges associated with coral
187 taxonomy ^{86,87}.

188

189 Platforms for screening large numbers of individuals for increased thermotolerance have been
190 developed in the form of standardized, mobile, and inexpensive acute heat stress assays, such
191 as the Coral Bleaching Automated Stress System (CBASS) ^{40,47,88–90}. The underlying premise is
192 that corals that exhibit increased thermal tolerance in acute assays are also more resistant and/or
193 resilient during natural heat stress events ^{40,89}. Indeed, considerable variation in thermotolerance
194 can be found and resolved among coral colonies from the same and disparate sites using such
195 short-term heat stress assays ^{40,42,61}. The genetic factors underlying such differences in stress
196 tolerance are, however, not fully understood or identified⁴². Newly available CRISPR technology
197 has been shown to work in corals and could be used to help understand the genetic basis of
198 thermotolerance differences, in addition to offering the potential for engineering tolerant
199 populations in the future, provided all safety requirements are satisfied ^{91,92}. However, the genetic
200 factors underpinning stress tolerance in corals are complex: it is a polygenic trait with potentially
201 100s of genes involved, although a subset of conserved genes exist that could form suitable
202 targets for exploration and/or manipulation ^{42,60,93,94}.

203

204 Colonies from warmer and often geographically distinct regions could provide higher gains in
205 thermotolerance when considered for relocation or selective breeding, but there are associated
206 risks, including potential dilution of local gene pools. Local environments exert selection pressures
207 across a multitude of environmental parameters (so-called environmental mosaics), of which
208 temperature is only one. The translocation of colonies across large geographic distances is
209 therefore problematic as transplanted corals might face a foreign environment, potentially
210 resulting in reduced fitness, reduced competitiveness and ultimately reduced survival ^{95,96}. In
211 addition, the lack of clarity around coral taxonomy and the inherent plastic morphology raises
212 concerns regarding crosses of colonies assigned to the same species from disparate locations.

213

214 Substantial differences in thermal tolerance can already be found at smaller geographic scales
215 (for example at the reef scale), as coral reefs provide a plethora of **microhabitats [G]** that select
216 for more thermotolerant genotypes, resulting in large phenotypic variation within local populations
217 available for exploitation ^{40,78,97}. Although this variation might not extend to the greatest extremes
218 of tolerance possible for a given species, it avoids the risks associated with the introduction of
219 foreign genotypes into local populations. Consequently, the identification of locally adapted
220 colonies with high thermotolerance for selective breeding approaches could be the most prudent
221 approach to follow, at least in the case of broadcast spawning corals ⁹⁸. Selected colonies from
222 different microenvironments could be maintained in local land-based nurseries, allowing for
223 controlled conditions and crosses as well as the rearing of larvae to the pre-settlement stage to
224 increase survivorship ⁹⁹. Unwanted domestication effects, such as a growth advantage of corals
225 that do better under aquaria conditions, could make it challenging to maintain coral genotypes
226 that “thrive” under environmental extremes, though ³³. Thus, the use of pre-settlement larvae
227 screened for increased thermotolerance for deployment in local reefs and subsequent
228 environmental selection of suitable genotypes might be the most promising approach ¹⁰⁰.
229

230 **[H1] Adaptive Strategies of Symbiodiniaceae**

231 Symbiodiniaceae are the primary photosymbionts of shallow water tropical coral species ¹⁰¹.
232 These microalgae reside within the cells of their coral host and provide photosynthates that
233 broadly cover the energy needs of the coral in return for a light-rich, sheltered environment and
234 the provisioning of CO₂ and other micronutrients ^{102–104}. Modern corals and Symbiodiniaceae co-
235 diversified in the Jurassic Period (about 160 mya), linking the success of reef ecosystems to this
236 symbiosis ¹⁰¹. The Symbiodiniaceae family is likely comprised of hundreds of species ^{101,105,106}
237 with comparative genomic data revealing extensive divergence among and within genera
238 ^{101,107,108}. The substantial diversification of the family is explained by the high level of host
239 specialization and fidelity, even under environmental extremes ^{109–111}.
240

241 The coral–Symbiodiniaceae endosymbiosis is particularly sensitive to heat and light stress, which
242 together can cause coral bleaching and subsequent mortality ^{12,15}. Although shifts in the dominant
243 Symbiodiniaceae towards more thermotolerant species are observed ¹¹², most novel associations
244 do not persist ^{109,113}. Thus, considerable effort has been placed on understanding stress tolerance
245 limits among Symbiodiniaceae and how these factors influence coral holobiont performance ^{114–}
246 ¹¹⁶. As a result, there is a growing appreciation for the diverse mechanisms that Symbiodiniaceae
247 use to acclimate and adapt to a changing environment on their own as well as in concert with their
248 hosts ^{106,115,117,118}. For example, cultured Symbiodiniaceae cells are highly plastic with short-term
249 acclimatory responses in growth, motility, gene expression, and photochemistry observed in
250 response to changes in temperature, light, pH, salinity and nutrient content ^{119–122}. Similar
251 responses have been recorded in algal communities on coral reefs ^{42,123}.
252

253 Symbiodiniaceae also possess many traits that favor rapid evolutionary adaptation, including
254 short generation times, both sexual and asexual reproductive modes, and genomic adaptive
255 precursors, such as extensive functional enrichments, mobile elements and RNA editing

256 107,122,124,125. Interactions with corals and the loss or gain of a symbiotic lifestyle are also predicted
257 to drive evolutionary change ¹⁰⁸. Even in the absence of their cnidarian hosts, experimental
258 evolution protocols over several years have induced major genetic and phenotypic changes in
259 cultured algae ¹²⁶. In nature, Symbiodiniaceae typically exhibit a more pronounced population
260 structure than corals ¹²⁷, signifying geographic isolation, local selection, and opportunities for local
261 adaptation ^{40,42,110,111,127–129}.

262
263 Variation in the extent of symbiont specificity among coral life stages is important for predicting
264 the potential for different coral species to change their symbiont communities through acclimatory
265 processes like switching or shuffling, which involve reorganizing the symbiont community to favor
266 dominance of heat tolerant taxa ^{130–132}. Coral larvae and juveniles are more plastic in their
267 association with different Symbiodiniaceae compared with adult colonies ^{133–135} and these could
268 be the critical life stages for focused manipulative experiments (**Table 1, Fig. 2**). Indeed,
269 manipulation of host-symbiont pairings might be a critical component of both natural and artificial
270 adaptive strategies. However, there is limited evidence for successful long-term manipulation
271 ^{48,136}. Short-term manipulation of the coral-algal symbiosis can be experimentally achieved at early
272 life stages via symbiont seeding from the environmental pool or by providing new symbiosis
273 opportunities (for example, by sourcing conspecific symbionts from geographically distant
274 environments, or novel symbionts from distinct host species) ^{137–141}. Further approaches include
275 the stress-hardening of adult corals with more invasive methods, including implanting cores of
276 coral tissue containing heat-tolerant symbionts ¹³⁶ or via direct genetic engineering of the
277 symbionts themselves ¹⁴². However, Symbiodiniaceae seem intractable to such manipulation at
278 present ¹⁴³.

279
280 Ultimately the utility of symbiont community manipulations is dependent on whether alterations
281 are heritable ^{144,145}. If induced changes do not persist across coral generations, then they will only
282 function as temporary stopgaps. Although there is evidence to suggest a component of altered
283 Symbiodiniaceae community composition is heritable ¹⁴⁵, in the vast majority of cases examined,
284 associations appear to be highly specific ^{101,109–111}. Any symbiont shuffling that takes place
285 naturally (or artificially after thermal bleaching or exposure during larval or juvenile stages) does
286 not persist across generations. Instead, the original symbiont composition is restored when
287 environmental conditions return to normal, or after juveniles develop mature immune systems ^{146–}
288 ¹⁴⁹.

289
290 The exception to the rule of reversion to the original community is evident when stressful
291 conditions persist for extended periods or recur with high frequency ¹¹². In such cases, the balance
292 shifts such that stress-tolerant Symbiodiniaceae are favored over metabolically optimized
293 symbionts, and novel species can remain as the numerically dominant partner. With the frequency
294 and intensity of bleaching events increasing, it has been argued that environmental conditions on
295 reefs could soon favor thermally tolerant, novel symbionts ¹³⁶. Such replacement seems to be
296 underway in the Caribbean, with the spread of the heat-tolerant, potentially invasive *Durusdinium*
297 *trenchii* ^{112,150}. Among Pacific reefs with bi-annual or annual repeat bleaching, symbiont
298 communities have also already been observed to shift toward dominance of heat-tolerant
299 Symbiodiniaceae ^{151,152}, though it is unknown whether such shifts persist across generations.

300 However, even the most resilient symbionts are expected to provide no more than 2°C of
301 additional thermal tolerance to the coral holobiont, a threshold that will likely be exceeded in the
302 tropics within the next 100 years¹⁵³. The benefit might increase if holobionts evolve to reach
303 greater optima in this period⁷⁶, although the pace of such evolutionary processes under these
304 conditions is unknown.

305
306 Even if altered symbiont communities could persist across generations, there are practical limits
307 to artificially manipulating associations on a large scale. The inoculation and/or manipulation of
308 individual coral adults might only provide single-colony scale resolution due to labor-intensive
309 methods (**Table 1**). The most promising, scalable approach is to introduce coral larvae or
310 juveniles to alternative algal symbionts while rearing large batches as part of ongoing restoration
311 projects. However, mortality at these early life stages is high (up to >99% for larvae), though the
312 numbers are improving with technological advances^{99,154}. Such efforts might be able to seed
313 struggling reefs with thermally tolerant coral individuals in the future. Currently, the most efficient
314 means of manipulating symbiont communities at scale remains—ironically—anthropogenic
315 climate change.

316

317 **[H1] Adaptive Strategies of Prokaryotes**

318 Prokaryotes (bacteria and archaea) have a crucial role in the health, fitness, and ecological
319 adaptation of metaorganisms^{44,155–158}. The coral microbiome (the community of bacteria and
320 archaea) is influenced by the surrounding environmental conditions, host species, age, and size
321 of colonies^{159–162}. These community diversity patterns reflect the dynamic relationship between
322 prokaryotes and environmental conditions, which are hypothesized to select for the most
323 advantageous coral holobiont composition under a given setting, termed the Coral Probiotic
324 Hypothesis¹⁶³. The concept of microbiome flexibility⁴⁴ acknowledges that the capacity for
325 microbial change differs among coral species, with some species showing large microbiome
326 changes across adverse environmental regimes, while others exhibit highly conserved bacterial
327 assemblages^{47,162,164}. Despite such flexibility, a number of taxonomic groups are found
328 consistently associated with corals, such as *Endozoicomonas*^{165,166}. Some of these taxa correlate
329 with health, like *Roseobacter* spp.^{167,168} or *Pseudoalteromonas* spp.^{167,169}, and others with
330 disease, like *Vibrio* spp.^{170,171} or *Rhodobacter* spp.¹⁷², although the role or function for the majority
331 of prokaryotes is unknown.

332

333 Manipulative studies employing reciprocal coral transplants or microbial manipulations that
334 correlate changes with increased coral stress tolerance^{47,53,162,169,173} highlight that microbiome
335 alteration could provide an alternate route to ecological adaptation, facilitating rapid responses of
336 corals to changing environments^{44,47,53}. Microbiome flexibility to adapt to adverse environmental
337 conditions underlies the **Beneficial Microorganisms for Corals [G]** (BMC) concept that centers
338 around the identification of microbes that promote coral health and their subsequent utilization as
339 **coral probiotics [G]**^{37,174}. Manipulating the coral microbiome is less about the mitigation of a
340 specific impact, but focuses on increasing overall health, based on the premise that a healthier
341 organism is more resilient when subjected to stress^{52,175}. Such health improvements could

342 mitigate an array of impacts that include thermal stress, pathogen challenge, and poor water
343 quality ⁵². Accordingly, the premise underlying BMCs is to reboot an altered and dysbiotic
344 microbiome caused by environmental stress ^{162,176}, with the intention to outcompete opportunistic
345 and detrimental microbes to restore or rehabilitate the altered microbiome and its microbial-
346 mediated functions to the coral holobiont ^{37,162} (**Table 1, Fig. 2**).

347
348 Several proof-of-concept studies now demonstrate that exposure of corals to BMCs can improve
349 coral health through potentially mitigating stress and toxic compounds or controlling pathogens,
350 although the underlying molecular mechanisms remain to be determined ^{52,177,178}. For instance,
351 BMCs were successfully applied to ameliorate impacts caused by pathogens ¹⁷⁹ or toxic
352 compounds ^{177,178}. Bacterial BMCs to mitigate coral thermal stress have been genomically and
353 biochemically screened for beneficial functions including pathogen-targeted antimicrobial activity,
354 reactive oxygen species (ROS) mitigation, dimethylsulfoniopropionate (DMSP) breakdown, and
355 nitrogen cycling ^{169,180}. BMCs can even promote coral bleaching recovery and prevent coral
356 mortality through mitigating post-heat stress disorder syndrome, possibly through bacterial
357 reactive oxygen species scavenging, coral host transcriptional reprogramming, and provisioning
358 of alternate nutrition sources to boost coral energetics ¹⁸⁰.

359
360 BMC treatments appear to be most successful when applied during the stress exposure.
361 However, BMCs are not retained for long periods of time, therefore likely requiring to be re-
362 administered at times of stress ^{52,180}, although retention might differ by life stage ¹⁵⁹. The
363 application of coral prebiotics [G] could also assist corals in the selection and retention of BMCs.
364 Prebiotic application with or without administered BMCs during bleaching events could promote
365 active enrichment of the coral microbiome as well as facilitate association with beneficial microbes
366 (**Table 1, Fig. 2**). In addition, the development of strategies to scale up BMC delivery is required.
367 Such upscaling might be achieved through immobilization of microbial cells and/or slowing their
368 temporal release through attachment to biocompatible carriers, as well as bioencapsulation in
369 prey or uptake through heterotrophic feeding ^{52,181}. Although existing genetic engineering
370 techniques are easily applied to bacterial isolates derived from corals, they should be restrained
371 to a laboratory context, as the effects that such altered genetic variants could exhibit in the highly
372 complex and diverse coral reef environment (for example, interaction with pathogens) are
373 unknown ¹⁸²⁻¹⁸⁴. Accordingly, coral microbiome manipulative approaches in reef sites should focus
374 on utilization of microbes (bacteria) from the native environment.

375

376 [H1] Adaptive Strategies of Viruses

377 Viruses can contribute to the evolution of their hosts and are critically important for the functioning
378 of marine ecosystems ¹⁸⁵. A mechanistic understanding of the direct role of viruses in holobiont
379 acclimation or adaptation is lacking, but there is evidence that viruses have a role in coral health,
380 disease, or stress (thermal) tolerance ¹⁸⁶⁻¹⁸⁹. One explanation could lie in bacteriophages – the
381 most abundant members of the coral metaorganism – controlling the abundance of specific
382 bacterial strains through lysis [G], and thereby shaping the structure of the microbiome and its
383 functional landscape ^{183,190}.

384

385 In humans and mice, viral predation of bacteria selects the bacterial strains that are able to
386 colonize an animal host upon invasion ^{191,192}. When the lytic removal of bacterial strains is
387 selective against pathogens, the viral predation effectively creates a form of immunity that is
388 extremely plastic ^{193,194}. Evidence suggests that in a similar way, coral-associated viruses prey on
389 detrimental bacteria that grow when stimulated by competitor turf algae ¹⁹⁵. Selective viral
390 predation of bacterial strains causes viral-host coevolution that could be a strong force shaping
391 the coral microbiome and, thereby affecting coral holobiont adaptability ⁴⁴. Yet, the specific
392 mechanisms underpinning these interactions are unknown, as well as how common such patterns
393 are.

394

395 Another way in which bacterial viruses can shape the microbiome, and by extension the genetic
396 and genomic makeup of the coral holobiont, is through lateral gene transfer ¹⁹⁶. Two main modes
397 of viral-based genetic transfer occur, one when random fragments of bacterial DNA are packed
398 into viral particles, and the other when specific regions of bacterial chromosomes that flank
399 integrated phage sequences are transferred. In both cases, lateral gene transfer can bring
400 benefits analogous to sexual reproduction, such as increasing fitness and compensating for
401 detrimental mutations in populations that replicate exclusively clonally ¹⁹⁷. Therefore, viral-
402 mediated increase in genetic exchange is expected to facilitate bacterial, and by extension
403 microbiome, adaptation to changing conditions. However, coral reef phages could also transfer
404 bacterial virulence genes that enable pathogen invasion of coral tissues and cause disease ^{198,199}.
405 Indeed, transitions in viral community composition have been associated with a number of coral
406 diseases ^{189,200}. However, little is known about the factors that determine how frequently coral-
407 associate viruses transfer genes with beneficial or pathogenic effects to the coral host. The coral
408 virome also contains abundant and diverse eukaryotic viruses ¹⁹⁶, which become more abundant
409 during bleaching ¹⁸⁷, although cause versus consequence is unknown. Specifically, viruses
410 infecting Symbiodiniaceae could have a direct effect on coral thermal sensitivity, potentially by
411 increasing rates of predation at high temperatures ^{186,201,202}.

412

413 The application of viruses for coral acclimation and adaptation could take two main (but not
414 exclusive) routes (**Table 1, Fig. 2**). First, viral therapy could help boost stress tolerance ¹⁸⁶
415 pending the successful isolation and culturing of such viral associates. Similarly, phage therapy
416 could be used to control coral diseases when a bacterial pathogen can be identified. Second,
417 phages could be employed to improve the efficacy of BMCs across a suite of applications (for
418 example, to mitigate thermal stress, disease, or oil spill impacts). The application of viruses with
419 BMCs in a "dual benefit approach" to target specific pathogens and improve coral holobiont health
420 is probably the most realistic near-future application. In principle, phages could be used as a tool
421 to transfer desirable genes to members of the BMC consortia (or other entities of the coral
422 holobiont), making them more efficient in colonizing the coral holobiont or stabilizing associations.
423 However, this method would involve adding **genetically modified organisms [G]** (GMOs) to natural
424 ecosystems, an approach less likely to gain support. Alternatively, native coral-associated viruses
425 could have their abundances manipulated, increasing their natural rates of predation or gene
426 transfer, depending on the desired effect on the bacterial community. This approach relies on a
427 better understanding of the functions of each microbiome and virome member ¹⁹⁰.

428
429 Phage therapy is, in particular, a promising tool for restoration or rehabilitation processes because
430 it addresses the problem of scaling - through their high replication rates and population expansion,
431 phages presumably would distribute even at the reef scale ^{203,204}. For example, phage therapy
432 has successfully prevented bacterial induced photosystem inhibition in Symbiodiniaceae ²⁰⁵ and
433 inhibited white plague disease progression in *Favia fava* in aquaria and in the field ^{206,207}.
434 However, the possibilities for applying phage therapy on corals in the wild are very limited because
435 of unanticipated off-target effects and potential of uncontrolled expansion. The application of
436 phage therapy to treat coral diseases is also constrained because for most coral diseases the
437 causative pathogens have not been identified and many diseases might not be caused by a single
438 distinct pathogen ²⁰⁸⁻²¹¹.

439
440 There are several essential questions that need to be answered if viruses are to be applied in
441 coral restoration efforts. Perhaps the most pressing need is the reconstruction of virus-host
442 infection networks of coral species targeted for manipulation ²¹². Most of the viruses identified in
443 coral microbiomes have not been matched with a host, prokaryotic or eukaryotic, although
444 available data suggest that many perceived viral-host associations need to be reevaluated
445 ^{187,196,200}. For instance, Hepadnaviridae are typically ascribed to be vertebrate-specific but have
446 been found associated with coral genera ¹⁹⁶. This lack of knowledge about virus-host relationships
447 prevents the identification of viruses that are potentially beneficial for coral, either through
448 modulating the associated microbiome and its genetic pathways, affecting the response to stress
449 (including Symbiodiniaceae), or encoding genes that improve microbiome function. The
450 reconstruction of phage-bacteria infection networks will also contribute to constraining the
451 possibility of off-target infections and recombination in phage therapy. By knowing how similar an
452 introduced phage is to the resident phages, the risk of moving unwanted genetic material through
453 lateral gene transfer can be reduced ²¹³. Such risk reduction is especially important because many
454 resident phages encode bacterial virulence genes, which must not be accessible to bacteria that
455 are strong colonizers of coral mucus and tissues ^{196,199,214}. Applying native phages that originate
456 from the same or similar coral reef and coral holobiont that will be treated reduces the risk of off-
457 target effects.

458

459 **[H1] ~~A coral holobiont~~ An adaptive intervention framework**

460 Societal need to retain healthy coral reefs under climate change is driving a new era of innovation
461 in reef science, evidenced by global multidisciplinary exploration of approaches to enhance coral
462 resilience ^{30,85,215}. From a pragmatic point of view, restoration—trying to recreate reefs as they
463 once were—is largely unachievable, but also would likely not provide future resilience as climate
464 stressors persist and intensify²¹⁶. Rather, enhancing current functional and/or genetic diversity
465 through **environmental rehabilitation [G]** to allow reefs to thrive under the new set of conditions
466 should be aimed for. Embedding this central philosophy is critical since reef conditions are likely
467 to worsen before they improve, even if the Paris Agreement goals are achieved ^{30,217}. Intervention
468 measures aimed at increasing coral resilience will hopefully retain enough functional coral reefs
469 to assist in long-term recovery. The following sections outline how such intervention measures

470 could look like, how they complement and can be integrated with existing practices, and how their
471 efficacy can be monitored in the wild.
472

473 ***[H2] Extending the coral holobiont natural adaptive capacity***

474 Intervention approaches have the greatest potential, feasibility, and readiness if harnessing the
475 natural adaptive capacity of corals, thereby employing naturally evolved solutions that are tried-
476 and-tested in reef ecosystems. They also avoid many of the concerns associated with genetic
477 and/or technological engineering, and therefore, governance and social license. Risks will vary
478 depending on the intervention approach with, for example, environmental hardening possessing
479 less risk though with limited longer term resilience gains than selective breeding approaches,
480 which directly interfere with coral population structures. Risks associated with the use of probiotics
481 or other means of microbiome manipulation can be reduced if native microbiome partners are
482 used, though how long these treatments persist or whether these approaches require repeated
483 application. It is essential to assess their longer-term benefits to determine their efficacy,
484 applicability, and the best way to combine or integrate them with other techniques (**Table 1, Fig.**
485 **2**). Nature-based solutions still entail manipulation of biological interactions amongst holobiont
486 partners, albeit avoiding any use of GMOs. Gaining a better understanding of the interactions
487 between holobiont member species is necessary to identify and maximize synergistic effects
488 through targeted combinations of different intervention methods, whereby all combinations are
489 theoretically possible (**Fig. 3**). Selective breeding, for instance, can provide substantial increases
490 in temperature resilience and could be further boosted through environmental hardening and/or
491 the provisioning of probiotics and alternative algal symbiont strains.

492
493 The combination of different approaches does not rely on additional infrastructure beyond what
494 is required for their independent implementation. Given the differences in practicality, scalability,
495 and the time required for the interventions to take effect, it might be most efficient to combine
496 technologies at different levels. Although selectively bred corals likely [have the highest potential
497 for resilience gains and scalability in the long run, their production is costly and scaling up is
498 mostly achieved through propagation in the wild ^{136,218,219}. Implementation will therefore require
499 natural populations to persist to provide enough coral cover for efficient natural reproduction and
500 the preservation of ecosystem services. Initially, more scalable methods such as probiotics and
501 symbiont manipulations could be used to increase resilience of the natural populations, ensuring
502 sufficient coral cover to maintain coral reef function and providing enough colonies for efficient
503 sexual reproduction and sufficient genetic diversity until beneficial alleles reach critical densities
504 in the populations (**Fig. 3, Fig. 4**). Currently however, it is unknown to what degree interventions
505 centered around the coral holobiont translate into observable reef-level effects or the time that is
506 required for holobiont-targeted interventions to manifest at the reef level. Addressing this gap in
507 knowledge between holobiont-centered interventions to meet reef ecological scale goals is a key
508 priority for global restoration efforts ²²⁰.
509

510 **[H2] A scaled adaptive intervention framework**

511
512 Coral propagation provides the fundamental practical framework needed to accelerate reef
513 restoration, where the goal is to deliver coral functional diversity (in the form of taxonomic diversity
514 that covers the different functions provided by reef-building corals) at a scale that exceeds natural
515 recovery (as well as mortality) rates. Most coral restoration practices worldwide, however, still rely
516 on asexual fragmentation-based propagation of individual genetic (or phenotypic) lines, and
517 therefore do not address restoration of functional genetic diversity³⁹. Asexual fragmentation is a
518 method utilized to boost living coral tissue within degraded reef areas quickly. It can also be
519 implemented in situ by non-specialist groups, in particular through innovations enabling scalability
520 of nursery-based propagation and out-planting rates^{221–223}. Propagation and outplanting success
521 is generally high (>75-90%)^{39,223,224}, but survivorship can decline precipitously over time^{224,225},
522 especially where other factors—such as disproportionately high corallivore rates—are not
523 simultaneously mitigated. Success is further confounded where practices often operate without
524 knowledge of the inherent genetic and functional diversity, and hence do not increase the
525 resilience of coral produced and even run the risk of adaptive bottlenecks in the long-term^{41,218}.
526 Consequently, effective repopulation rests on capturing sufficient genetic and functional diversity
527 to resist stochastic environmental change^{222,226,227}. As such, sexual propagation techniques to
528 maximize genetic recombination of parents—and hence adaptive potential—through either
529 controlled (such as selective breeding amongst genotypes) or uncontrolled (such as mass larval-
530 based seeding of out-plant structures) approaches^{84,137,218,228} represent an essential and
531 necessary pipeline, not only for coral reef restoration, but rehabilitation.

532
533 Coral propagation approaches are now becoming tuned towards adaptive capacity. New
534 diagnostic tools can be deployed to identify within-species diversity for more informed propagation
535 decision-making^{40,41}, and ex situ spawning aquarium systems can be employed to overcome
536 limited larval supply imposed by annual coral spawning events²²⁹ (**Fig. 4**). Efforts in the Indo-
537 Pacific have demonstrated how propagating within-species genetic diversity is important to
538 ensuring efforts against transient heat waves⁸⁹. This work suggests that new tools capable of
539 high throughput diagnostics of tolerance to different stressors, such as Coral Bleaching
540 Automated Stress System assays⁴⁰, could become critical components in scaling coral
541 restoration effectiveness and informing targeted breeding approaches (**Fig. 4**). Resolving the
542 extent of local coral holobiont diversity—and how it is inter-dispersed amongst sites via
543 connectivity and reproduction patterns^{230,231}—provides a logical basis for ensuring that active
544 propagation efforts exploit the maximum available range of genetic diversity and coral functional
545 performance (**Fig. 4**). Efforts are rapidly gearing towards overcoming technical and
546 methodological constraints for selective breeding approaches based on large-scale sexual
547 propagation²¹⁸.

548
549 Alongside these efforts to enhance coral resilience, it is still important to mitigate the impact of
550 environmental parameters, such as water quality, that are broadly linked to reef resilience and
551 directly implicated in coral bleaching and disease susceptibility^{24–26,162}. Interventions to enhance
552 the stress tolerance of corals are unlikely to succeed without addressing local environmental
553 conditions. Moreover, the technology to grow more resilient coral colonies is available (**Fig. 2**),

554 but colony and reef growth will not naturally speed up. Better integration of current reef
555 management practices and scaled adaptive approaches are required (**Fig. 3**). Local stressors,
556 such as water quality and overfishing, act synergistically with climate change and represent
557 important targets for intervention measures to counter some of the effects of global climate
558 change ^{24,25,27}. Measures to improve water quality or reduce overfishing, alongside the
559 management of other environmental drivers of reef decline, should be prioritized alongside the
560 more manipulative coral holobiont-centric intervention measures presented here.
561

562 **[H2] Standardization and monitoring success**

563 Despite the prospect of combining emergent technologies with tried-and-tested approaches,
564 standardized protocols must be developed and made available for broad application, which
565 should become more available in the coming years, or are already in place ²¹⁸ (**Fig. 2, Fig. 4**).
566 Restoration and/or rehabilitation will likely benefit from operational frameworks that can adopt
567 'best of both worlds' practices. More specialized, manipulative (and likely costly) solutions to be
568 applied when reefs are severely endangered or degraded, in balance with broader scale
569 measures that aim to maintain reef health and do not require sophisticated instrumentation or
570 knowledge to implement (such as monitoring water quality) (**Fig. 3**). In addition, not all intervention
571 measures are needed everywhere and all the time. Rather, standardized surveys to determine
572 reef state, for example through measurements of coral cover, reproductive potential, and thermal
573 tolerance, can then provide a list of indicated actions (**Fig. 3**). In all likelihood, no unified approach
574 exists that could be used globally because local conditions can either amplify or reduce climate
575 change impacts and therefore must be considered ²⁷.

576
577 The continuous monitoring to determine success and identify potential risks or side effects of
578 applied approaches is also critically important. While survival following bleaching events will
579 ultimately determine how successful the applied intervention measures were in increasing
580 resilience, the identification of potential risks will require more active measures. For instance,
581 when using selectively bred corals, coral population structure should be monitored to determine
582 how frequencies of beneficial alleles increase over time or whether outbreeding depression can
583 be observed. Similarly, the application of coral probiotics requires regular monitoring to assess
584 any changes in the microbial community assemblage and potential re-application of the treatment.
585

586 **[H1] Summary and future perspectives**

587 Coral reefs globally are rapidly degrading, requiring the development and implementation of novel
588 intervention strategies to mitigate the impacts of ongoing climate change and environmental
589 degradation. Research activities are attempting to extend the adaptive capacity of reef-forming
590 corals through novel tools, methods, and environments that are studied to increase the survival
591 of corals under more extreme or variable conditions. A particular emphasis on the coral holobiont
592 as the functional biological unit provides a more complete and better understanding of coral
593 functioning while opening the door for novel strategies and targets to harness and maximize the
594 adaptive capacity of corals and the reefs they build to survive climate change. These emerging

595 approaches need to consider and be tailored towards the different reef, environmental, and
596 ecological conditions. Implementing an adaptive intervention framework tailored around nature-
597 based solutions requires standardized methodology, safety assessments, and analytical routines
598 for consistent and most effective utilization and global coordination.

599
600 Work on the following four areas could accelerate implementation of the framework described
601 here, starting with increasing our understanding of the role of other coral holobiont entities as
602 targets of adaptive intervention. For instance, endolithic algae (like *Ostreobium*) can translocate
603 fixed carbon to the coral during coral bleaching, potentially providing resilience to thermal stress
604 by offering alternate energy provision to sustain coral function^{232,233}. Similarly, corallicolids
605 (Apicomplexa) live inside coral tissues and are only second in abundance to Symbiodiniaceae,
606 but their ecology is still unclear²³⁴. Second, extreme environments such be utilized as sources of
607 discovery regarding adaptive mechanisms, powerful probiotics, and the biological, ecological,
608 physico-chemical characteristics underlying coral reef refuges^{77,235–237}. Third, knowledge from
609 real-world case studies must be expanded: it is currently unknown how much ‘manipulation’ within
610 a given population is ideal ecologically or acceptable from a management perspective. In other
611 words, the relative contribution of selectively bred vs. randomly bred coral colonies must be
612 investigated, along with the amount of manipulation needed to exert a measurable effect at the
613 reef level. This knowledge is likely to be highly variable for reefs from different localities³⁶. Similar
614 considerations apply for assisted gene flow or seeding coral larvae approaches.

615
616
617 Finally, the application of manipulative approaches will be most effective through standardization
618 and coordination of efforts, which will also allow assessment of feasibility, efficacy, and risks in a
619 much quicker and coherent way^{40,105,238}. Predictions of coral survival are imperfect. All reefs and
620 corals are subject to changing environments, and it is not clear if the best predictor of future coral
621 colony survival is their past survival. We need to derive standardized analytical and decision-
622 frameworks that are accurate, easy to implement, and reliable at predicting measures that provide
623 corals and reefs with the highest chance of survival. Such standardization will be reliant on a
624 global data- and knowledge base to enable comparative (meta-)analyses and provide a long-term
625 defined and coordinated strategy to catalyze and ensure effective coral reef conservation.

626

627 **References**

- 628 1. Fisher, R. *et al.* Species richness on coral reefs and the pursuit of convergent global estimates. *Curr.*
629 *Biol.* **25**, 500–505 (2015).
- 630 2. Costanza, R. *et al.* Changes in the global value of ecosystem services. *Glob. Environ. Change* **26**,
631 152–158 (2014).
- 632 3. Moberg, F. & Folke, C. Ecological goods and services of coral reef ecosystems. *Ecol. Econ.* **29**,
633 215–233 (1999).
- 634 4. Wilkinson, C. *Status of Coral Reefs of the World: 2008*. (2008).
- 635 5. Spalding, M. *et al.* Mapping the global value and distribution of coral reef tourism. *Mar. Policy* **82**,
636 104–113 (2017).
- 637 6. Hoegh-Guldberg, O. Climate change, coral bleaching and the future of the world’s coral reefs.

- 638 *Marine and Freshwater Research* **50**, 839–866 (1999).
- 639 **Projects loss and degradation of coral reefs on a global scale before it became common**
- 640 **knowledge.**
- 641 7. Hughes, T. P. *et al.* Global warming transforms coral reef assemblages. *Nature* **556**, 492–496
- 642 (2018).
- 643 8. Porter, J. W. & Meier, O. W. Quantification of Loss and Change in Floridian Reef Coral Populations.
- 644 *American Zoologist* vol. 32 625–640 (1992).
- 645 9. Ruzicka, R. R. *et al.* Temporal changes in benthic assemblages on Florida Keys reefs 11 years after
- 646 the 1997/1998 El Niño. *Mar. Ecol. Prog. Ser.* **489**, 125–141 (2013).
- 647 10. Somerfield, P. J. *et al.* Changes in coral reef communities among the Florida Keys, 1996–2003.
- 648 *Coral Reefs* **27**, 951–965 (2008).
- 649 11. Lapointe, B. E., Brewton, R. A., Herren, L. W., Porter, J. W. & Hu, C. Nitrogen enrichment, altered
- 650 stoichiometry, and coral reef decline at Looe Key, Florida Keys, USA: a 3-decade study. *Mar. Biol.*
- 651 **166**, 108 (2019).
- 652 12. Suggett, D. J. & Smith, D. J. Coral bleaching patterns are the outcome of complex biological and
- 653 environmental networking. *Global Change Biology* (2019) doi:10.1111/gcb.14871.
- 654 13. Hughes, T. P. *et al.* Spatial and temporal patterns of mass bleaching of corals in the Anthropocene.
- 655 *Science* **359**, 80–83 (2018).
- 656 14. Lesser, M. P. Coral Bleaching: Causes and Mechanisms. *Coral Reefs: An Ecosystem in Transition*
- 657 405–419 (2011) doi:10.1007/978-94-007-0114-4_23.
- 658 15. Räddecker, N. *et al.* Heat stress destabilizes symbiotic nutrient cycling in corals. *Proc. Natl. Acad. Sci.*
- 659 *U. S. A.* **118**, (2021).
- 660 **Demonstrates that algal symbionts cease photosynthate transfer to coral hosts under heat**
- 661 **stress long before visual signs of bleaching (symbiont loss) become evident.**
- 662 16. Allen, M. R. *et al.* Framing and Context. in *Global Warming of 1.5°C. An IPCC Special Report on the*
- 663 *impacts of global warming of 1.5°C above pre-industrial levels and related global greenhouse gas*
- 664 *emission pathways, in the context of strengthening the global response to the threat of climate*
- 665 *change, sustainable development, and efforts to eradicate poverty* (eds. [Masson-Delmotte *et al.*])
- 666 vol. In Press. (2018).
- 667 17. Gattuso, J.-P. *et al.* OCEANOGRAPHY. Contrasting futures for ocean and society from different
- 668 anthropogenic CO₂ emissions scenarios. *Science* **349**, aac4722 (2015).
- 669 18. Hughes, D. J. *et al.* Coral reef survival under accelerating ocean deoxygenation. *Nat. Clim. Chang.*
- 670 **10**, 296–307 (2020).
- 671 19. Röthig, T. *et al.* Anthropogenically caused salinity changes impact marine organisms and
- 672 ecosystems. *submitted* (2021).
- 673 20. Morris, L. A., Voolstra, C. R., Quigley, K. M., Bourne, D. G. & Bay, L. K. Nutrient Availability and
- 674 Metabolism Affect the Stability of Coral-Symbiodiniaceae Symbioses. *Trends Microbiol.* **27**, 678–689
- 675 (2019).
- 676 21. Muller, E. M., Sartor, C., Alcaraz, N. I. & van Woesik, R. Spatial Epidemiology of the Stony-Coral-
- 677 Tissue-Loss Disease in Florida. (2020) doi:10.3389/fmars.2020.00163.
- 678 22. Hughes, T. P. *et al.* Climate change, human impacts, and the resilience of coral reefs. *Science* **301**,
- 679 929–933 (2003).
- 680 23. Nyström, M., Folke, C. & Moberg, F. Coral reef disturbance and resilience in a human-dominated
- 681 environment. *Trends Ecol. Evol.* **15**, 413–417 (2000).
- 682 24. Wiedenmann, J. *et al.* Nutrient enrichment can increase the susceptibility of reef corals to bleaching.
- 683 *Nat. Clim. Chang.* **3**, 160–164 (2012).
- 684 25. D'Angelo, C. & Wiedenmann, J. Impacts of nutrient enrichment on coral reefs: new perspectives and
- 685 implications for coastal management and reef survival. *Current Opinion in Environmental*
- 686 *Sustainability* **7**, 82–93 (2014).

- 687 26. Thurber, R. L. V. *et al.* Chronic nutrient enrichment increases prevalence and severity of coral
688 disease and bleaching. *Global Change Biology* vol. 20 544–554 (2014).
- 689 27. Donovan, M. K. *et al.* Local conditions magnify coral loss after marine heatwaves. *Science* **372**, 977–
690 980 (2021).
- 691 28. Climate change widespread, rapid, and intensifying – IPCC. *Working Group I Report of the IPCC’s*
692 *Sixth Assessment Report (AR6)* <https://www.ipcc.ch/2021/08/09/ar6-wg1-20210809-pr/> (2021).
- 693 29. Radchuk, V. *et al.* Adaptive responses of animals to climate change are most likely insufficient. *Nat.*
694 *Commun.* **10**, 3109 (2019).
- 695 30. Kleypas, J. *et al.* Designing a blueprint for coral reef survival. *Biol. Conserv.* **257**, 109107 (2021).
- 696 31. Gattuso, J.-P. *et al.* Ocean Solutions to Address Climate Change and Its Effects on Marine
697 Ecosystems. *Frontiers in Marine Science* **5**, 337 (2018).
- 698 32. Hoegh-Guldberg, O., Kennedy, E. V., Beyer, H. L., McClennen, C. & Possingham, H. P. Securing a
699 Long-term Future for Coral Reefs. *Trends Ecol. Evol.* **33**, 936–944 (2018).
- 700 33. Zoccola, D. *et al.* The World Coral Conservatory (WCC): A Noah’s ark for corals to support survival
701 of reef ecosystems. *PLoS Biol.* **18**, e3000823 (2020).
- 702 34. Kleinhaus, K. *et al.* Science, Diplomacy, and the Red Sea’s Unique Coral Reef: It’s Time for Action.
703 *Frontiers in Marine Science* **7**, 90 (2020).
- 704 35. van Oppen, M. J. H., Oliver, J. K., Putnam, H. M. & Gates, R. D. Building coral reef resilience
705 through assisted evolution. *Proc. Natl. Acad. Sci. U. S. A.* **112**, 2307–2313 (2015).
- 706 36. Baums, I. B. *et al.* Considerations for maximizing the adaptive potential of restored coral populations
707 in the western Atlantic. *Ecol. Appl.* **29**, e01978 (2019).
- 708 37. Peixoto, R. S., Sweet, M. & Bourne, D. G. Customized Medicine for Corals. *Frontiers in Marine*
709 *Science* **6**, 686 (2019).
- 710 38. Rinkevich, B. The Active Reef Restoration Toolbox is a Vehicle for Coral Resilience and Adaptation
711 in a Changing World. *J. Mar. Sci. Eng.* **7**, 201 (2019).
- 712 39. Boström-Einarsson, L. *et al.* Coral restoration - A systematic review of current methods, successes,
713 failures and future directions. *PLoS One* **15**, e0226631 (2020).
- 714 40. Voolstra, C. R. *et al.* Standardized short-term acute heat stress assays resolve historical differences
715 in coral thermotolerance across microhabitat reef sites. *Glob. Chang. Biol.* **26**, 4328–4343 (2020).
716 **Highlights the potential of mobile acute heat stress assays to resolve fine-scale differences in**
717 **coral thermotolerance, suitable for large-scale identification of resilient genotypes/reefs for**
718 **conservation and restoration approaches.**
- 719 41. Parkinson, J. E. *et al.* Molecular tools for coral reef restoration: Beyond biomarker discovery.
720 *Conservation Letters* **13**, e12687 (2020).
- 721 42. Voolstra, C. R. *et al.* Contrasting heat stress response patterns of coral holobionts across the Red
722 Sea suggest distinct mechanisms of thermal tolerance. *Mol. Ecol.* (2021) doi:10.1111/mec.16064.
- 723 43. Sweet, M. & Brown, B. Coral responses to anthropogenic stress in the twenty-first century: An
724 ecophysiological perspective. in *Oceanography and Marine Biology - An Annual Review* 271–314
725 (CRC Press, 2016). doi:10.1201/9781315368597-6.
- 726 44. Voolstra, C. R. & Ziegler, M. Adapting with Microbial Help: Microbiome Flexibility Facilitates Rapid
727 Responses to Environmental Change. *Bioessays* **42**, e2000004 (2020).
728 **Proposes microbiome flexibility as a mechanism to aid adaptation to environmental change**
729 **and posits that capacity for dynamic restructuring of the microbiome is host specific.**
- 730 45. Jaspers, C. *et al.* Resolving structure and function of metaorganisms through a holistic framework
731 combining reductionist and integrative approaches. *Zoology* **133**, 81–87 (2019).
- 732 46. Torda, G. *et al.* Rapid adaptive responses to climate change in corals. *Nat. Clim. Chang.* **7**, 627–636
733 (2017).
- 734 47. Ziegler, M., Seneca, F. O., Yum, L. K., Palumbi, S. R. & Voolstra, C. R. Bacterial community
735 dynamics are linked to patterns of coral heat tolerance. *Nat. Commun.* **8**, 14213 (2017).

- 736 **Provides the first putative link between bacterial community composition and coral heat**
737 **tolerance.**
- 738 48. Morgans, C. A., Hung, J. Y., Bourne, D. G. & Quigley, K. M. Symbiodiniaceae probiotics for use in
739 bleaching recovery. *Restor. Ecol.* **28**, 282–288 (2020).
- 740 49. Liew, Y. J. *et al.* Intergenerational epigenetic inheritance in reef-building corals. *Nat. Clim. Chang.*
741 **10**, 254–259 (2020).
- 742 50. Craggs, J. *et al.* Inducing broadcast coral spawning ex situ: Closed system mesocosm design and
743 husbandry protocol. *Ecol. Evol.* **7**, 11066–11078 (2017).
- 744 51. Camp, E. F., Schoepf, V. & Suggett, D. J. How can “Super Corals” facilitate global coral reef survival
745 under rapid environmental and climatic change? *Glob. Chang. Biol.* **24**, 2755–2757 (2018).
- 746 52. Peixoto, R. S. *et al.* Coral Probiotics: Premise, Promise, Prospects. *Annu Rev Anim Biosci* **9**, 265–
747 288 (2021).
- 748 **Reviews coral probiotics and critical assessment of applicability.**
- 749 53. Doering, T. *et al.* Towards enhancing coral heat tolerance: a “microbiome transplantation” treatment
750 using inoculations of homogenized coral tissues. *Microbiome* **9**, 102 (2021).
- 751 54. Devlin-Durante, M. K., Miller, M. W., Caribbean Acropora Research Group, Precht, W. F. & Baums,
752 I. B. How old are you? Genet age estimates in a clonal animal. *Mol. Ecol.* **25**, 5628–5646 (2016).
- 753 55. Irwin, A. *et al.* Age and intraspecific diversity of resilient Acropora communities in Belize. *Coral Reefs*
754 **36**, 1111–1120 (2017).
- 755 56. Palumbi, S. R., Barshis, D. J., Traylor-Knowles, N. & Bay, R. A. Mechanisms of reef coral resistance
756 to future climate change. *Science* **344**, 895–898 (2014).
- 757 **Demonstrates that acclimation and adaptation contribute to coral thermal tolerance and**
758 **climate resistance at about equal contribution.**
- 759 57. Barott, K. L. *et al.* Coral bleaching response is unaltered following acclimatization to reefs with
760 distinct environmental conditions. *Proc. Natl. Acad. Sci. U. S. A.* **118**, (2021).
- 761 58. Thomas, L., López, E. H., Morikawa, M. K. & Palumbi, S. R. Transcriptomic resilience, symbiont
762 shuffling, and vulnerability to recurrent bleaching in reef-building corals. *Mol. Ecol.* **28**, 3371–3382
763 (2019).
- 764 59. Bellantuono, A. J., Granados-Cifuentes, C., Miller, D. J., Hoegh-Guldberg, O. & Rodriguez-Lanetty,
765 M. Coral thermal tolerance: tuning gene expression to resist thermal stress. *PLoS One* **7**, e50685
766 (2012).
- 767 60. Barshis, D. J. *et al.* Genomic basis for coral resilience to climate change. *Proc. Natl. Acad. Sci. U. S.*
768 *A.* **110**, 1387–1392 (2013).
- 769 61. Savary, R. *et al.* Fast and pervasive transcriptomic resilience and acclimation of extremely heat-
770 tolerant coral holobionts from the northern Red Sea. *Proc. Natl. Acad. Sci. U. S. A.* **118**, (2021).
- 771 62. Liew, Y. J. *et al.* Epigenome-associated phenotypic acclimatization to ocean acidification in a reef-
772 building coral. *Sci Adv* **4**, eaar8028 (2018).
- 773 63. Durante, M. K., Baums, I. B., Williams, D. E., Vohsen, S. & Kemp, D. W. What drives phenotypic
774 divergence among coral clonemates of *Acropora palmata*? *Mol. Ecol.* **28**, 3208–3224 (2019).
- 775 64. Rodríguez-Casariego, J. A. *et al.* Genome-wide DNA methylation analysis reveals a conserved
776 epigenetic response to seasonal environmental variation in the staghorn coral *Acropora cervicornis*.
777 *Front. Mar. Sci.* **7**, (2020).
- 778 65. Putnam, H. M. & Gates, R. D. Preconditioning in the reef-building coral *Pocillopora damicornis* and
779 the potential for trans-generational acclimatization in coral larvae under future climate change
780 conditions. *J. Exp. Biol.* **218**, 2365–2372 (2015).
- 781 66. Putnam, H. M., Davidson, J. M. & Gates, R. D. Ocean acidification influences host DNA methylation
782 and phenotypic plasticity in environmentally susceptible corals. *Evol. Appl.* **9**, 1165–1178 (2016).
- 783 67. Putnam, H. M., Ritson-Williams, R., Cruz, J. A., Davidson, J. M. & Gates, R. D. Environmentally-
784 induced parental or developmental conditioning influences coral offspring ecological performance.

- 785 *Sci. Rep.* **10**, 13664 (2020).
- 786 68. Drury, C. *et al.* Genomic variation among populations of threatened coral: *Acropora cervicornis*. *BMC*
787 *Genomics* **17**, 286 (2016).
- 788 69. Bay, R. A., Rose, N. H., Logan, C. A. & Palumbi, S. R. Genomic models predict successful coral
789 adaptation if future ocean warming rates are reduced. *Sci Adv* **3**, e1701413 (2017).
- 790 70. Prada, C. *et al.* Empty Niches after Extinctions Increase Population Sizes of Modern Corals. *Curr.*
791 *Biol.* **26**, 3190–3194 (2016).
- 792 71. Van Oppen, M. J. H., Souter, P., Howells, E. J., Heyward, A. & Berkelmans, R. Novel Genetic
793 Diversity Through Somatic Mutations: Fuel for Adaptation of Reef Corals? *Diversity* **3**, 405–423
794 (2011).
- 795 72. Vasquez Kuntz, K. L. *et al.* Juvenile corals inherit mutations acquired during the parent's lifespan.
796 *bioRxiv* 2020.10.19.345538 (2020) doi:10.1101/2020.10.19.345538.
- 797 73. Matz, M. V., Treml, E. A., Aglyamova, G. V. & Bay, L. K. Potential and limits for rapid genetic
798 adaptation to warming in a Great Barrier Reef coral. *PLoS Genet.* **14**, e1007220 (2018).
- 799 74. Guest, J. R. *et al.* Contrasting patterns of coral bleaching susceptibility in 2010 suggest an adaptive
800 response to thermal stress. *PLoS One* **7**, e33353 (2012).
- 801 75. Coles, S. L. *et al.* Evidence of acclimatization or adaptation in Hawaiian corals to higher ocean
802 temperatures. *PeerJ* **6**, e5347 (2018).
- 803 76. Sully, S., Burkepile, D. E., Donovan, M. K., Hodgson, G. & van Woesik, R. A global analysis of coral
804 bleaching over the past two decades. *Nat. Commun.* **10**, 1264 (2019).
- 805 77. Camp, E. F. *et al.* The Future of Coral Reefs Subject to Rapid Climate Change: Lessons from
806 Natural Extreme Environments. *Frontiers in Marine Science* **5**, 4 (2018).
- 807 78. Oliver, T. A. & Palumbi, S. R. Do fluctuating temperature environments elevate coral thermal
808 tolerance? *Coral Reefs* **30**, 429–440 (2011).
- 809 79. Morgan, K. M., Perry, C. T., Smithers, S. G., Johnson, J. A. & Daniell, J. J. Evidence of extensive
810 reef development and high coral cover in nearshore environments: implications for understanding
811 coral adaptation in turbid settings. *Sci. Rep.* **6**, 29616 (2016).
- 812 80. Middlebrook, R., Hoegh-Guldberg, O. & Leggat, W. The effect of thermal history on the susceptibility
813 of reef-building corals to thermal stress. *J. Exp. Biol.* **211**, 1050–1056 (2008).
- 814 81. Brown, B. E., Dunne, R. P., Edwards, A. J., Sweet, M. J. & Phongsuwan, N. Decadal environmental
815 'memory' in a reef coral? *Mar. Biol.* **162**, 479–483 (2015).
- 816 82. Dixon, G., Liao, Y., Bay, L. K. & Matz, M. V. Role of gene body methylation in acclimatization and
817 adaptation in a basal metazoan. *Proc. Natl. Acad. Sci. U. S. A.* **115**, 13342–13346 (2018).
- 818 83. Humanes, A. *et al.* An Experimental Framework for Selectively Breeding Corals for Assisted
819 Evolution. *Frontiers in Marine Science* **8**, 626 (2021).
- 820 84. Dixon, G. B. *et al.* Genomic determinants of coral heat tolerance across latitudes. *Science* **348**,
821 1460–1462 (2015).
- 822 **Demonstrates applicability of assisted evolution via selective breeding.**
- 823 85. van Oppen, M. J. H. *et al.* Shifting paradigms in restoration of the world's coral reefs. *Glob. Chang.*
824 *Biol.* **23**, 3437–3448 (2017).
- 825 86. Fukami, H. *et al.* Conventional taxonomy obscures deep divergence between Pacific and Atlantic
826 corals. *Nature* **427**, 832–835 (2004).
- 827 87. Voolstra, C. R. *et al.* Consensus guidelines for advancing coral holobiont genome and specimen
828 voucher deposition. *Front. Mar. Sci.* **8**, 1029 (2021).
- 829 88. Seneca, F. O. & Palumbi, S. R. The role of transcriptome resilience in resistance of corals to
830 bleaching. *Mol. Ecol.* **24**, 1467–1484 (2015).
- 831 89. Morikawa, M. K. & Palumbi, S. R. Using naturally occurring climate resilient corals to construct
832 bleaching-resistant nurseries. *Proc. Natl. Acad. Sci. U. S. A.* **116**, 10586–10591 (2019).
- 833 90. Evensen, N. R., Fine, M., Perna, G., Voolstra, C. R. & Barshis, D. J. Remarkably high and consistent

- 834 tolerance of a Red Sea coral to acute and chronic thermal stress exposures. *Limnol. Oceanogr.*
835 (2021) doi:10.1002/lno.11715.
- 836 91. Cleves, P. A., Strader, M. E., Bay, L. K., Pringle, J. R. & Matz, M. V. CRISPR/Cas9-mediated
837 genome editing in a reef-building coral. *Proc. Natl. Acad. Sci. U. S. A.* **115**, 5235–5240 (2018).
- 838 92. Cleves, P. A. *et al.* Reduced thermal tolerance in a coral carrying CRISPR-induced mutations in the
839 gene for a heat-shock transcription factor. *Proc. Natl. Acad. Sci. U. S. A.* **117**, 28899–28905 (2020).
- 840 93. Fuller, Z. L. *et al.* Population genetics of the coral *Acropora millepora*: Toward genomic prediction of
841 bleaching. *Science* **369**, (2020).
- 842 94. Yetsko, K. *et al.* Genetic differences in thermal tolerance among colonies of threatened coral
843 *Acropora cervicornis*: potential for adaptation to increasing temperature. *Mar. Ecol. Prog. Ser.* **646**,
844 45–68 (2020).
- 845 95. Kenkel, C. D., Almanza, A. T. & Matz, M. V. Fine-scale environmental specialization of reef-building
846 corals might be limiting reef recovery in the Florida Keys. *Ecology* **96**, 3197–3212 (2015).
- 847 96. D'Angelo, C. *et al.* Local adaptation constrains the distribution potential of heat-tolerant
848 *Symbiodinium* from the Persian/Arabian Gulf. *ISME J.* **9**, 2551–2560 (2015).
- 849 97. Safaie, A. *et al.* High frequency temperature variability reduces the risk of coral bleaching. *Nat.*
850 *Commun.* **9**, 1671 (2018).
- 851 98. Quigley, K. M., Bay, L. K. & van Oppen, M. J. H. Genome-wide SNP analysis reveals an increase in
852 adaptive genetic variation through selective breeding of coral. *Mol. Ecol.* **29**, 2176–2188 (2020).
- 853 99. Craggs, J., Guest, J., Bulling, M. & Sweet, M. Ex situ co culturing of the sea urchin, *Mespilia globulus*
854 and the coral *Acropora millepora* enhances early post-settlement survivorship. *Sci. Rep.* **9**, 12984
855 (2019).
- 856 100. Quigley, K. M. *et al.* Variability in Fitness Trade-Offs Amongst Coral Juveniles With Mixed Genetic
857 Backgrounds Held in the Wild. *Frontiers in Marine Science* **8**, 161 (2021).
- 858 101. LaJeunesse, T. C. *et al.* Systematic Revision of Symbiodiniaceae Highlights the Antiquity and
859 Diversity of Coral Endosymbionts. *Curr. Biol.* **28**, 2570-2580.e6 (2018).
- 860 **Provides a revised coral symbiont taxonomy and shows that Symbiodiniaceae diversification**
861 **coincides with the radiation of reef-building corals.**
- 862 102. Muscatine, L. The role of symbiotic algae in carbon and energy flux in reef corals. *Coral Reefs* **25**,
863 (1990).
- 864 103. Trench & RK. Microalgal-invertebrate symbiosis, a review. *Endocytobiosis Cell Res.* **9**, 135–175
865 (1993).
- 866 104. Pogoreutz, C. *et al.* The coral holobiont highlights the dependence of cnidarian animal hosts on their
867 associated microbes. in *Cellular Dialogues in the Holobiont* (eds. Bosch, T. C. G. & Hadfield, M. G.)
868 91–118 (CRC Press, 2020). doi:10.1201/9780429277375-7.
- 869 105. Hume, B. C. C. *et al.* SymPortal: A novel analytical framework and platform for coral algal symbiont
870 next-generation sequencing ITS2 profiling. *Mol. Ecol. Resour.* **19**, 1063–1080 (2019).
- 871 106. Decelle, J. *et al.* Worldwide Occurrence and Activity of the Reef-Building Coral Symbiont
872 *Symbiodinium* in the Open Ocean. *Curr. Biol.* **28**, 3625-3633.e3 (2018).
- 873 107. Aranda, M. *et al.* Genomes of coral dinoflagellate symbionts highlight evolutionary adaptations
874 conducive to a symbiotic lifestyle. *Sci. Rep.* **6**, 39734 (2016).
- 875 108. González-Pech, R. A., Bhattacharya, D., Ragan, M. A. & Chan, C. X. Genome Evolution of Coral
876 Reef Symbionts as Intracellular Residents. *Trends Ecol. Evol.* **34**, 799–806 (2019).
- 877 109. Hume, B. C. C., Mejia-Restrepo, A., Voolstra, C. R. & Berumen, M. L. Fine-scale delineation of
878 Symbiodiniaceae genotypes on a previously bleached central Red Sea reef system demonstrates a
879 prevalence of coral host-specific associations. *Coral Reefs* **39**, 583–601 (2020).
- 880 110. Howells, E. J. *et al.* Corals in the hottest reefs in the world exhibit symbiont fidelity not flexibility. *Mol.*
881 *Ecol.* **29**, 899–911 (2020).
- 882 111. Turnham, K. E., Wham, D. C., Sampayo, E. & LaJeunesse, T. C. Mutualistic microalgae co-diversify

- 883 with reef corals that acquire symbionts during egg development. *ISME J.* (2021)
884 doi:10.1038/s41396-021-01007-8.
- 885 112. Grottoli, A. G. *et al.* The cumulative impact of annual coral bleaching can turn some coral species
886 winners into losers. *Glob. Chang. Biol.* **20**, 3823–3833 (2014).
- 887 113. LaJeunesse, T. C., Smith, R. T., Finney, J. & Oxenford, H. Outbreak and persistence of opportunistic
888 symbiotic dinoflagellates during the 2005 Caribbean mass coral 'bleaching' event. *Proceedings of*
889 *the Royal Society B: Biological Sciences* vol. 276 4139–4148 (2009).
- 890 114. Grégoire, V., Schmacka, F., Coffroth, M. A. & Karsten, U. Photophysiological and thermal tolerance
891 of various genotypes of the coral endosymbiont *Symbiodinium* sp. (Dinophyceae). *J. Appl. Phycol.*
892 **29**, 1893–1905 (2017).
- 893 115. Quigley, K. M., Baker, A. C., Coffroth, M. A., Willis, B. L. & van Oppen, M. J. H. Bleaching
894 Resistance and the Role of Algal Endosymbionts. in *Coral Bleaching: Patterns, Processes, Causes*
895 *and Consequences* (eds. van Oppen, M. J. H. & Lough, J. M.) 111–151 (Springer International
896 Publishing, 2018). doi:10.1007/978-3-319-75393-5_6.
- 897 116. Ziegler, M., Arif, C. & Voolstra, C. R. Symbiodiniaceae Diversity in Red Sea Coral Reefs & Coral
898 Bleaching. in *Coral Reefs of the Red Sea* (eds. Voolstra, C. R. & Berumen, M. L.) 69–89 (Springer
899 International Publishing, 2019). doi:10.1007/978-3-030-05802-9_5.
- 900 117. Suggett, D. J., Warner, M. E. & Leggat, W. Symbiotic Dinoflagellate Functional Diversity Mediates
901 Coral Survival under Ecological Crisis. *Trends Ecol. Evol.* **32**, 735–745 (2017).
- 902 118. Hume, B. C. C. *et al.* Ancestral genetic diversity associated with the rapid spread of stress-tolerant
903 coral symbionts in response to Holocene climate change. *Proc. Natl. Acad. Sci. U. S. A.* **113**, 4416–
904 4421 (2016).
- 905 119. Ochsenkühn, M. A., Röthig, T., D'Angelo, C., Wiedenmann, J. & Voolstra, C. R. The role of
906 floridoside in osmoadaptation of coral-associated algal endosymbionts to high-salinity conditions. *Sci*
907 *Adv* **3**, e1602047 (2017).
- 908 120. Baumgarten, S. *et al.* Integrating microRNA and mRNA expression profiling in *Symbiodinium*
909 *microadriaticum*, a dinoflagellate symbiont of reef-building corals. *BMC Genomics* **14**, 704 (2013).
- 910 121. Klein, S. G. *et al.* *Symbiodinium* mitigate the combined effects of hypoxia and acidification on a
911 noncalcifying cnidarian. *Glob. Chang. Biol.* **23**, 3690–3703 (2017).
- 912 122. Liew, Y. J., Li, Y., Baumgarten, S., Voolstra, C. R. & Aranda, M. Condition-specific RNA editing in
913 the coral symbiont *Symbiodinium microadriaticum*. *PLOS Genetics* vol. 13 e1006619 (2017).
- 914 123. Warner, M. E. & Suggett, D. J. The Photobiology of *Symbiodinium* spp.: Linking Physiological
915 Diversity to the Implications of Stress and Resilience. in *The Cnidaria, Past, Present and Future: The*
916 *world of Medusa and her sisters* (eds. Goffredo, S. & Dubinsky, Z.) 489–509 (Springer International
917 Publishing, 2016). doi:10.1007/978-3-319-31305-4_30.
- 918 124. Levin, R. A. *et al.* Sex, Scavengers, and Chaperones: Transcriptome Secrets of Divergent
919 *Symbiodinium* Thermal Tolerances. *Mol. Biol. Evol.* **33**, 3032 (2016).
- 920 125. Nand, A. *et al.* Genetic and spatial organization of the unusual chromosomes of the dinoflagellate
921 *Symbiodinium microadriaticum*. *Nat. Genet.* **53**, 618–629 (2021).
- 922 126. Buerger, P. *et al.* Heat-evolved microalgal symbionts increase coral bleaching tolerance. *Sci Adv* **6**,
923 eaba2498 (2020).
- 924 127. Thornhill, D. J., Howells, E. J., Wham, D. C., Steury, T. D. & Santos, S. R. Population genetics of
925 reef coral endosymbionts (*Symbiodinium*, Dinophyceae). *Molecular Ecology* vol. 26 2640–2659
926 (2017).
- 927 128. LaJeunesse, T. C. *et al.* Long-standing environmental conditions, geographic isolation and host-
928 symbiont specificity influence the relative ecological dominance and genetic diversification of coral
929 endosymbionts in the genus *Symbiodinium*. *J. Biogeogr.* **37**, 785–800 (2010).
- 930 129. Parkinson, J. E. *et al.* Gene Expression Variation Resolves Species and Individual Strains among
931 Coral-Associated Dinoflagellates within the Genus *Symbiodinium*. *Genome Biol. Evol.* **8**, 665–680

- 932 (2016).
- 933 130. Baker, A. C. Flexibility and Specificity in Coral-Algal Symbiosis: Diversity, Ecology, and
934 Biogeography of *Symbiodinium*. *Annu. Rev. Ecol. Evol. Syst.* **34**, 661–689 (2003).
- 935 131. Boulotte, N. M. *et al.* Exploring the Symbiodinium rare biosphere provides evidence for symbiont
936 switching in reef-building corals. *ISME J.* **10**, 2693–2701 (2016).
- 937 132. Ziegler, M., Eguíluz, V. M., Duarte, C. M. & Voolstra, C. R. Rare symbionts may contribute to the
938 resilience of coral-algal assemblages. *ISME J.* **12**, 161–172 (2018).
- 939 133. Mies, M., Sumida, P. Y. G., Rädcker, N. & Voolstra, C. R. Marine Invertebrate Larvae Associated
940 with Symbiodinium: A Mutualism from the Start? *Frontiers in Ecology and Evolution* vol. 5 (2017).
- 941 134. Cumbo, V. R., Baird, A. H. & van Oppen, M. J. H. The promiscuous larvae: flexibility in the
942 establishment of symbiosis in corals. *Coral Reefs* **32**, 111–120 (2013).
- 943 135. Quigley, K. M., Willis, B. L. & Bay, L. K. Heritability of the Symbiodinium community in vertically- and
944 horizontally-transmitting broadcast spawning corals. *Sci. Rep.* **7**, 8219 (2017).
- 945 136. National Academies of Sciences, Engineering, and Medicine. *A Research Review of Interventions to*
946 *Increase the Persistence and Resilience of Coral Reefs*. (The National Academies Press, 2019).
947 doi:10.17226/25279.
- 948 **Reviews restoration interventions, detailing latest emerging technologies and approaches.**
- 949 137. Quigley, K. M., Randall, C. J., van Oppen, M. J. H. & Bay, L. K. Assessing the role of historical
950 temperature regime and algal symbionts on the heat tolerance of coral juveniles. *Biol. Open* **9**,
951 (2020).
- 952 138. McIlroy, S. E. *et al.* The effects of Symbiodinium (Pyrrhophyta) identity on growth, survivorship, and
953 thermal tolerance of newly settled coral recruits. *J. Phycol.* **52**, 1114–1124 (2016).
- 954 139. Thornhill, D. J., Daniel, M. W., LaJeunesse, T. C., Schmidt, G. W. & Fitt, W. K. Natural infections of
955 aposymbiotic *Cassiopea xamachana* scyphistomae from environmental pools of *Symbiodinium*. *J.*
956 *Exp. Mar. Bio. Ecol.* **338**, 50–56 (2006).
- 957 140. Coffroth, M. A., Lewis, C. F., Santos, S. R. & Weaver, J. L. Environmental populations of symbiotic
958 dinoflagellates in the genus *Symbiodinium* can initiate symbioses with reef cnidarians. *Curr. Biol.* **16**,
959 R985-7 (2006).
- 960 141. Fujise, L. *et al.* Unlocking the phylogenetic diversity, primary habitats, and abundances of free-living
961 Symbiodiniaceae on a coral reef. *Mol. Ecol.* **30**, 343–360 (2021).
- 962 142. Levin, R. A. *et al.* Engineering Strategies to Decode and Enhance the Genomes of Coral Symbionts.
963 *Front. Microbiol.* **8**, 1220 (2017).
- 964 143. Chen, J. E., Barbrook, A. C., Cui, G., Howe, C. J. & Aranda, M. The genetic intractability of
965 *Symbiodinium microadriaticum* to standard algal transformation methods. *PLoS One* **14**, e0211936
966 (2019).
- 967 144. Sheykhal, S. *et al.* Robustness to extinction and plasticity derived from mutualistic bipartite
968 ecological networks. *Sci. Rep.* **10**, 9783 (2020).
- 969 145. Quigley, K. M., Bay, L. K. & Willis, B. L. Leveraging new knowledge of Symbiodinium community
970 regulation in corals for conservation and reef restoration. *Mar. Ecol. Prog. Ser.* **600**, 245–253 (2018).
- 971 146. LaJeunesse, T. C. *et al.* Host–symbiont recombination versus natural selection in the response of
972 coral–dinoflagellate symbioses to environmental disturbance. *Proceedings of the Royal Society B:*
973 *Biological Sciences* vol. 277 2925–2934 (2010).
- 974 147. Poland, D. M. & Coffroth, M. A. Trans-generational specificity within a cnidarian–algal symbiosis.
975 *Coral Reefs* **36**, 119–129 (2017).
- 976 148. Sampayo, E. M. *et al.* Coral symbioses under prolonged environmental change: living near tolerance
977 range limits. *Sci. Rep.* **6**, 36271 (2016).
- 978 149. Abrego, D., VAN Oppen, M. J. H. & Willis, B. L. Onset of algal endosymbiont specificity varies
979 among closely related species of *Acropora* corals during early ontogeny. *Mol. Ecol.* **18**, 3532–3543
980 (2009).

- 981 150. Pettay, D. T., Wham, D. C., Smith, R. T., Iglesias-Prieto, R. & LaJeunesse, T. C. Microbial invasion
982 of the Caribbean by an Indo-Pacific coral zooxanthella. *Proc. Natl. Acad. Sci. U. S. A.* **112**, 7513–
983 7518 (2015).
- 984 151. Qin, Z. *et al.* Diversity of Symbiodiniaceae in 15 Coral Species From the Southern South China Sea:
985 Potential Relationship With Coral Thermal Adaptability. *Front. Microbiol.* **10**, 2343 (2019).
- 986 152. Claar, D. C. *et al.* Dynamic symbioses reveal pathways to coral survival through prolonged
987 heatwaves. *Nature Communications* vol. 11 (2020).
- 988 153. Lim, E.-P. *et al.* Continuation of tropical Pacific Ocean temperature trend may weaken extreme El
989 Niño and its linkage to the Southern Annular Mode. *Sci. Rep.* **9**, 17044 (2019).
- 990 154. Pollock, F. J. *et al.* Coral larvae for restoration and research: a large-scale method for rearing
991 *Acropora millepora* larvae, inducing settlement, and establishing symbiosis. *PeerJ* **5**, e3732 (2017).
- 992 155. McFall-Ngai, M. *et al.* Animals in a bacterial world, a new imperative for the life sciences. *Proc. Natl.*
993 *Acad. Sci. U. S. A.* **110**, 3229–3236 (2013).
- 994 156. Bosch, T. C. G. & McFall-Ngai, M. J. Metaorganisms as the new frontier. *Zoology* **114**, 185–190
995 (2011).
- 996 157. Robbins, S. J. *et al.* A genomic view of the reef-building coral *Porites lutea* and its microbial
997 symbionts. *Nat Microbiol* **4**, 2090–2100 (2019).
- 998 158. Bang, C. *et al.* Metaorganisms in extreme environments: do microbes play a role in organismal
999 adaptation? *Zoology* **127**, 1–19 (2018).
- 1000 159. Williams, A. D., Brown, B. E., Putschim, L. & Sweet, M. J. Age-Related Shifts in Bacterial Diversity in
1001 a Reef Coral. *PLoS One* **10**, e0144902 (2015).
- 1002 160. Roder, C., Bayer, T., Aranda, M., Kruse, M. & Voolstra, C. R. Microbiome structure of the fungid
1003 coral *Ctenactis echinata* aligns with environmental differences. *Mol. Ecol.* **24**, 3501–3511 (2015).
- 1004 161. Sweet, M. J., Brown, B. E., Dunne, R. P., Singleton, I. & Bulling, M. Evidence for rapid, tide-related
1005 shifts in the microbiome of the coral *Coelastrea aspera*. *Coral Reefs* **36**, 815–828 (2017).
- 1006 162. Ziegler, M. *et al.* Coral bacterial community structure responds to environmental change in a host-
1007 specific manner. *Nat. Commun.* **10**, 3092 (2019).
- 1008 163. Reshef, L., Koren, O., Loya, Y., Zilber-Rosenberg, I. & Rosenberg, E. The coral probiotic hypothesis.
1009 *Environ. Microbiol.* **8**, 2068–2073 (2006).
- 1010 164. Pogoreutz, C. *et al.* Dominance of *Endozoicomonas* bacteria throughout coral bleaching and
1011 mortality suggests structural inflexibility of the *Pocillopora verrucosa* microbiome. *Ecol. Evol.* **8**,
1012 2240–2252 (2018).
- 1013 165. Neave, M. J. *et al.* Differential specificity between closely related corals and abundant
1014 *Endozoicomonas* endosymbionts across global scales. *ISME J.* **11**, 186–200 (2017).
- 1015 166. Neave, M. J., Apprill, A., Ferrier-Pagès, C. & Voolstra, C. R. Diversity and function of prevalent
1016 symbiotic marine bacteria in the genus *Endozoicomonas*. *Appl. Microbiol. Biotechnol.* **100**, 8315–
1017 8324 (2016).
- 1018 167. Nissimov, J., Rosenberg, E. & Munn, C. B. Antimicrobial properties of resident coral mucus bacteria
1019 of *Oculina patagonica*. *FEMS Microbiol. Lett.* **292**, 210–215 (2009).
- 1020 168. Sharp, K. H., Sneed, J. M., Ritchie, K. B., Mcdaniel, L. & Paul, V. J. Induction of Larval Settlement in
1021 the Reef Coral *Porites astreoides* by a Cultivated Marine Roseobacter Strain. *Biol. Bull.* **228**, 98–107
1022 (2015).
- 1023 169. Rosado, P. M. *et al.* Marine probiotics: increasing coral resistance to bleaching through microbiome
1024 manipulation. *ISME J.* **13**, 921–936 (2019).
- 1025 170. Sunagawa, S. *et al.* Bacterial diversity and White Plague Disease-associated community changes in
1026 the Caribbean coral *Montastraea faveolata*. *ISME J.* **3**, 512–521 (2009).
- 1027 171. Ushijima, B., Smith, A., Aeby, G. S. & Callahan, S. M. *Vibrio owensii* induces the tissue loss disease
1028 *Montipora* white syndrome in the Hawaiian reef coral *Montipora capitata*. *PLoS One* **7**, e46717
1029 (2012).

- 1030 172. Mouchka, M. E., Hewson, I. & Harvell, C. D. Coral-associated bacterial assemblages: current
1031 knowledge and the potential for climate-driven impacts. *Integr. Comp. Biol.* **50**, 662–674 (2010).
- 1032 173. Glasl, B., Herndl, G. J. & Frade, P. R. The microbiome of coral surface mucus has a key role in
1033 mediating holobiont health and survival upon disturbance. *ISME J.* **10**, 2280–2292 (2016).
- 1034 174. Peixoto, R. S., Rosado, P. M., Leite, D. C. de A., Rosado, A. S. & Bourne, D. G. Beneficial
1035 Microorganisms for Corals (BMC): Proposed Mechanisms for Coral Health and Resilience. *Front.*
1036 *Microbiol.* **8**, 341 (2017).
- 1037 175. Mueller, E. A., Wisnoski, N. I., Peralta, A. L. & Lennon, J. T. Microbial rescue effects: How
1038 microbiomes can save hosts from extinction. *Funct. Ecol.* **34**, 2055–2064 (2020).
- 1039 176. Leite, D. C. A. *et al.* Coral Bacterial-Core Abundance and Network Complexity as Proxies for
1040 Anthropogenic Pollution. *Front. Microbiol.* **9**, 833 (2018).
- 1041 177. Fragoso Ados Santos, H. *et al.* Impact of oil spills on coral reefs can be reduced by bioremediation
1042 using probiotic microbiota. *Sci. Rep.* **5**, 18268 (2015).
- 1043 178. Silva, D. P. *et al.* Multi-domain probiotic consortium as an alternative to chemical remediation of oil
1044 spills at coral reefs and adjacent sites. *Microbiome* vol. 9 (2021).
- 1045 179. Welsh, R. M. *et al.* Alien vs. predator: bacterial challenge alters coral microbiomes unless controlled
1046 by Halobacteriovorax predators. *PeerJ* **5**, e3315 (2017).
- 1047 180. Santoro, E. P. *et al.* Coral microbiome manipulation elicits metabolic and genetic restructuring to
1048 mitigate heat stress and evade mortality. *Science Advances* (2021).
- 1049 181. Assis, J. M. *et al.* Delivering Beneficial Microorganisms for Corals: Rotifers as Carriers of Probiotic
1050 Bacteria. *Front. Microbiol.* **11**, 608506 (2020).
- 1051 182. Damjanovic, K., Blackall, L. L., Webster, N. S. & van Oppen, M. J. H. The contribution of microbial
1052 biotechnology to mitigating coral reef degradation. *Microb. Biotechnol.* **10**, 1236–1243 (2017).
- 1053 183. van Oppen, M. J. H. & Blackall, L. L. Coral microbiome dynamics, functions and design in a
1054 changing world. *Nat. Rev. Microbiol.* **17**, 557–567 (2019).
- 1055 184. Sweet, M. *et al.* Insights into the Cultured Bacterial Fraction of Corals. *mSystems* **6**, e0124920
1056 (2021).
- 1057 185. Brussaard, C. P. D., Baudoux, A.-C. & Rodríguez-Valera, F. Marine Viruses. in *The Marine*
1058 *Microbiome: An Untapped Source of Biodiversity and Biotechnological Potential* (eds. Stal, L. J. &
1059 Cretoiu, M. S.) 155–183 (Springer International Publishing, 2016). doi:10.1007/978-3-319-33000-
1060 6_5.
- 1061 186. Levin, R. A., Voolstra, C. R., Weynberg, K. D. & van Oppen, M. J. H. Evidence for a role of viruses in
1062 the thermal sensitivity of coral photosymbionts. *ISME J.* **11**, 808–812 (2017).
- 1063 187. Messyasz, A. *et al.* Coral Bleaching Phenotypes Associated With Differential Abundances of
1064 Nucleocytoplasmic Large DNA Viruses. *Frontiers in Marine Science* vol. 7 (2020).
- 1065 188. Thurber, R. L. V. *et al.* Metagenomic analysis indicates that stressors induce production of herpes-
1066 like viruses in the coral *Porites compressa*. *Proceedings of the National Academy of Sciences* **105**,
1067 18413–18418 (2008).
- 1068 189. Sweet, M. & Bythell, J. The role of viruses in coral health and disease. *J. Invertebr. Pathol.* **147**,
1069 136–144 (2017).
- 1070 190. Thurber, R. V., Payet, J. P., Thurber, A. R. & Correa, A. M. S. Virus–host interactions and their roles
1071 in coral reef health and disease. *Nat. Rev. Microbiol.* **15**, 205–216 (2017).
- 1072 **Reviews the role of viruses in coral holobiont biology.**
- 1073 191. Frazão, N., Sousa, A., Lässig, M. & Gordo, I. Horizontal gene transfer overrides mutation in
1074 *Escherichia coli* colonizing the mammalian gut. *Proc. Natl. Acad. Sci. U. S. A.* **116**, 17906–17915
1075 (2019).
- 1076 192. Lepage, P. *et al.* Dysbiosis in inflammatory bowel disease: a role for bacteriophages? *Gut* vol. 57
1077 424–425 (2008).
- 1078 193. Barr, J. J. *et al.* Bacteriophage adhering to mucus provide a non-host-derived immunity. *Proc. Natl.*

- 1079 *Acad. Sci. U. S. A.* **110**, 10771–10776 (2013).
- 1080 194. Silveira, C. B. & Rohwer, F. L. Piggyback-the-Winner in host-associated microbial communities. *npj*
- 1081 *Biofilms and Microbiomes* vol. 2 (2016).
- 1082 195. Roach, T. N. F. *et al.* A multiomic analysis of in situ coral-turf algal interactions. *Proc. Natl. Acad. Sci.*
- 1083 *U. S. A.* **117**, 13588–13595 (2020).
- 1084 196. Cárdenas, A. *et al.* Coral-Associated Viral Assemblages From the Central Red Sea Align With Host
- 1085 Species and Contribute to Holobiont Genetic Diversity. *Front. Microbiol.* **11**, 572534 (2020).
- 1086 197. Bondy-Denomy, J. & Davidson, A. R. When a virus is not a parasite: the beneficial effects of
- 1087 prophages on bacterial fitness. *J. Microbiol.* **52**, 235–242 (2014).
- 1088 198. Weynberg, K. D., Voolstra, C. R., Neave, M. J., Buerger, P. & van Oppen, M. J. H. From cholera to
- 1089 corals: Viruses as drivers of virulence in a major coral bacterial pathogen. *Sci. Rep.* **5**, 17889 (2015).
- 1090 199. Silveira, C. B. *et al.* Genomic and ecological attributes of marine bacteriophages encoding bacterial
- 1091 virulence genes. *BMC Genomics* **21**, 126 (2020).
- 1092 200. Soffer, N., Brandt, M. E., Correa, A. M. S., Smith, T. B. & Thurber, R. V. Potential role of viruses in
- 1093 white plague coral disease. *ISME J.* **8**, 271–283 (2014).
- 1094 201. Weynberg, K. D. *et al.* Prevalent and persistent viral infection in cultures of the coral algal
- 1095 endosymbiont Symbiodinium. *Coral Reefs* **36**, 773–784 (2017).
- 1096 202. Brüwer, J. D., Agrawal, S., Liew, Y. J., Aranda, M. & Voolstra, C. R. Association of coral algal
- 1097 symbionts with a diverse viral community responsive to heat shock. *BMC Microbiol.* **17**, 174 (2017).
- 1098 203. Jacquemot, L. *et al.* Therapeutic Potential of a New Jumbo Phage That Infects *Vibrio coralliilyticus*, a
- 1099 Widespread Coral Pathogen. *Front. Microbiol.* **9**, 2501 (2018).
- 1100 204. Efrony, R., Loya, Y., Bacharach, E. & Rosenberg, E. Phage therapy of coral disease. *Coral Reefs*
- 1101 **26**, 7–13 (2007).
- 1102 205. Cohen, Y., Joseph Pollock, F., Rosenberg, E. & Bourne, D. G. Phage therapy treatment of the coral
- 1103 pathogen *Vibrio coralliilyticus*. *Microbiologyopen* **2**, 64–74 (2013).
- 1104 206. Efrony, R., Atad, I. & Rosenberg, E. Phage therapy of coral white plague disease: properties of
- 1105 phage BA3. *Curr. Microbiol.* **58**, 139–145 (2009).
- 1106 207. Atad, I., Zvuloni, A., Loya, Y. & Rosenberg, E. Phage therapy of the white plague-like disease of
- 1107 *Favia fava* in the Red Sea. *Coral Reefs* **31**, 665–670 (2012).
- 1108 208. Sweet, M. J. & Bulling, M. T. On the Importance of the Microbiome and Pathobiome in Coral Health
- 1109 and Disease. *Frontiers in Marine Science* **4**, 9 (2017).
- 1110 209. Pollock, F. J., Morris, P. J., Willis, B. L. & Bourne, D. G. The urgent need for robust coral disease
- 1111 diagnostics. *PLoS Pathog.* **7**, e1002183 (2011).
- 1112 210. Lesser, M. P., Bythell, J. C., Gates, R. D., Johnstone, R. W. & Hoegh-Guldberg, O. Are infectious
- 1113 diseases really killing corals? Alternative interpretations of the experimental and ecological data. *J.*
- 1114 *Exp. Mar. Bio. Ecol.* **346**, 36–44 (2007).
- 1115 211. Roder, C., Arif, C., Daniels, C., Weil, E. & Voolstra, C. R. Bacterial profiling of White Plague Disease
- 1116 across corals and oceans indicates a conserved and distinct disease microbiome. *Molecular Ecology*
- 1117 vol. 23 965–974 (2014).
- 1118 212. Soffer, N., Zaneveld, J. & Vega Thurber, R. Phage-bacteria network analysis and its implication for
- 1119 the understanding of coral disease. *Environ. Microbiol.* **17**, 1203–1218 (2015).
- 1120 213. Ubeda, C. *et al.* Antibiotic-induced SOS response promotes horizontal dissemination of
- 1121 pathogenicity island-encoded virulence factors in staphylococci. *Mol. Microbiol.* **56**, 836–844 (2005).
- 1122 214. Cárdenas, A. *et al.* Excess labile carbon promotes the expression of virulence factors in coral reef
- 1123 bacterioplankton. *ISME J.* **12**, 59–76 (2018).
- 1124 215. Anthony, K. *et al.* New interventions are needed to save coral reefs. *Nat Ecol Evol* **1**, 1420–1422
- 1125 (2017).
- 1126 216. Allard, S. M. *et al.* Introducing the Mangrove Microbiome Initiative: Identifying Microbial Research
- 1127 Priorities and Approaches To Better Understand, Protect, and Rehabilitate Mangrove Ecosystems.

- 1128 *mSystems* **5**, (2020).
- 1129 217. Zickfeld, K. *et al.* Long-Term Climate Change Commitment and Reversibility: An EMIC
1130 Intercomparison. 5782–5809 (2013).
- 1131 218. Humanes, A. *et al.* A framework for selectively breeding corals for assisted evolution. *bioRxiv*
1132 2021.02.23.432469 (2021) doi:10.1101/2021.02.23.432469.
- 1133 219. National Academies of Sciences, Engineering, and Medicine, Division on Earth and Life Studies,
1134 Board on Life Sciences, Ocean Studies Board & Committee on Interventions to Increase the
1135 Resilience of Coral Reefs. *A Decision Framework for Interventions to Increase the Persistence and*
1136 *Resilience of Coral Reefs*. (National Academies Press, 2019). doi:10.17226/25424.
- 1137 220. Vardi, T. *et al.* Six priorities to advance the science and practice of coral reef restoration worldwide.
1138 *Restor. Ecol.* (2021).
- 1139 221. Page, C. A., Muller, E. M. & Vaughan, D. E. Microfragmenting for the successful restoration of slow
1140 growing massive corals. *Ecol. Eng.* **123**, 86–94 (2018).
- 1141 222. Schopmeyer, S. A. *et al.* Regional restoration benchmarks for *Acropora cervicornis*. *Coral Reefs* **36**,
1142 1047–1057 (2017).
- 1143 223. Suggett, D. J., Edmondson, J., Howlett, L. & Camp, E. F. Coralclip®: a low-cost solution for rapid
1144 and targeted out-planting of coral at scale. *Restor. Ecol.* **28**, 289–296 (2020).
- 1145 224. Woesik, R. *et al.* Differential survival of nursery-reared *Acropora cervicornis* outplants along the
1146 Florida reef tract. *Restor. Ecol.* **29**, (2021).
- 1147 225. Ware, M. *et al.* Survivorship and growth in staghorn coral (*Acropora cervicornis*) outplanting projects
1148 in the Florida Keys National Marine Sanctuary. *PLoS One* **15**, e0231817 (2020).
- 1149 226. Ladd, M. C., Shantz, A. A., Bartels, E. & Burkepile, D. E. Thermal stress reveals a genotype-specific
1150 tradeoff between growth and tissue loss in restored *Acropora cervicornis*. *Mar. Ecol. Prog. Ser.* **572**,
1151 129–139 (2017).
- 1152 227. Goergen, E. A. & Gilliam, D. S. Outplanting technique, host genotype, and site affect the initial
1153 success of outplanted *Acropora cervicornis*. *PeerJ* **6**, e4433 (2018).
- 1154 228. Chamberland, V. F. *et al.* New Seeding Approach Reduces Costs and Time to Outplant Sexually
1155 Propagated Corals for Reef Restoration. *Sci. Rep.* **7**, 18076 (2017).
- 1156 229. Craggs, J., Guest, J., Davis, M. & Sweet, M. Completing the life cycle of a broadcast spawning coral
1157 in a closed mesocosm. *Invertebr. Reprod. Dev.* **64**, 244–247 (2020).
- 1158 230. Hock, K. *et al.* Connectivity and systemic resilience of the Great Barrier Reef. *PLoS Biol.* **15**,
1159 e2003355 (2017).
- 1160 231. Quigley, K. M., Bay, L. K. & van Oppen, M. J. H. The active spread of adaptive variation for reef
1161 resilience. *Ecol. Evol.* **9**, 11122–11135 (2019).
- 1162 232. Sangsawang, L. *et al.* 13C and 15N assimilation and organic matter translocation by the endolithic
1163 community in the massive coral *Porites lutea*. *R Soc Open Sci* **4**, 171201 (2017).
- 1164 233. Pernice, M. *et al.* Down to the bone: the role of overlooked endolithic microbiomes in reef coral
1165 health. *ISME J.* **14**, 325–334 (2020).
- 1166 234. Kwong, W. K., Del Campo, J., Mathur, V., Vermeij, M. J. A. & Keeling, P. J. A widespread coral-
1167 infecting apicomplexan with chlorophyll biosynthesis genes. *Nature* **568**, 103–107 (2019).
- 1168 235. Fine, M., Gildor, H. & Genin, A. A coral reef refuge in the Red Sea. *Glob. Chang. Biol.* **19**, 3640–
1169 3647 (2013).
- 1170 236. Osman, E. O. *et al.* Thermal refugia against coral bleaching throughout the northern Red Sea. *Glob.*
1171 *Chang. Biol.* **24**, e474–e484 (2018).
- 1172 237. Camp, E. F. *et al.* Corals exhibit distinct patterns of microbial reorganisation to thrive in an extreme
1173 inshore environment. *Coral Reefs* **39**, 701–716 (2020).
- 1174 238. Grotoli, A. G. *et al.* Increasing comparability among coral bleaching experiments. *Ecol. Appl.* **31**,
1175 e02262 (2021).
- 1176 239. Putnam, H. M., Barott, K. L., Ainsworth, T. D. & Gates, R. D. The Vulnerability and Resilience of

- 1177 Reef-Building Corals. *Curr. Biol.* **27**, R528–R540 (2017).
- 1178 240. Hagedorn, M. & Spindler, R. The reality, use and potential for cryopreservation of coral reefs. *Adv.*
1179 *Exp. Med. Biol.* **753**, 317–329 (2014).
- 1180 241. Hagedorn, M. *et al.* Successful Demonstration of Assisted Gene Flow in the Threatened Coral
1181 *Acropora Palmata* Across Genetically-Isolated Caribbean Populations using Cryopreserved Sperm.
1182 *Cold Spring Harbor Laboratory* 492447 (2018) doi:10.1101/492447.
- 1183 242. Hagedorn, M., Spindler, R. & Daly, J. Cryopreservation as a Tool for Reef Restoration: 2019. *Adv.*
1184 *Exp. Med. Biol.* **1200**, 489–505 (2019).
- 1185 243. Daly, J. *et al.* Successful cryopreservation of coral larvae using vitrification and laser warming. *Sci.*
1186 *Rep.* **8**, 15714 (2018).
- 1187 244. Chakravarti, L. J., Beltran, V. H. & van Oppen, M. J. H. Rapid thermal adaptation in photosymbionts
1188 of reef-building corals. *Glob. Chang. Biol.* **23**, 4675–4688 (2017).
- 1189 245. Quigley, K. M., Alvarez Roa, C., Torda, G., Bourne, D. G. & Willis, B. L. Co-dynamics of
1190 Symbiodiniaceae and bacterial populations during the first year of symbiosis with *Acropora tenuis*
1191 juveniles. *Microbiologyopen* **9**, e959 (2020).
- 1192 246. Teplitski, M. & Ritchie, K. How feasible is the biological control of coral diseases? *Trends Ecol. Evol.*
1193 **24**, 378–385 (2009).
- 1194
- 1195

1196 **Acknowledgements**

1197 CRV acknowledges funding from the German Research Foundation (DFG), grants 433042944
1198 and 458901010. JEP acknowledges funding from the University of South Florida Research &
1199 Innovation Internal Awards Program, grant 0142687. KMQ acknowledges funding from the
1200 Australian Institute of Marine Science (AIMS). EMM was supported by the Mote Eminent
1201 Scholarship and the National Science Foundation (NSF) OCE-1452538. MA acknowledges
1202 funding from King Abdullah University of Science and Technology, grant FCC/1/1973-36-01.

1203

1204 **Author contributions**

1205 Researching data for article: CRV, RP, JEP, KMQ, CBS, MS, MA; substantial contribution to
1206 discussion of content: CRV, DJS, RP, JEP, KMQ, CBS, DGB, MA; writing: CRV, DJS, RP, JEP,
1207 KMQ, CBS, DGB, MA; review/editing of manuscript before submission: CRV, DJS, RP, JEP,
1208 KMQ, CBS, MS, EMM, DJB, DGB, MA

1209

1210 **Competing interests**

1211 The authors declare no competing interests.

1212

1213 **Peer review information**

1214 *Nature Reviews Earth & Environment* thanks [Referee#1 name], [Referee#2 name] and the other,
1215 anonymous, reviewer(s) for their contribution to the peer review of this work.

1216

1217 **Publisher's note**

1218 Springer Nature remains neutral with regard to jurisdictional claims in published maps and
1219 institutional affiliations.

1220

1221 **Key points**

- 1222 - Coral reefs are degrading globally from anthropogenic climate change and local environmental
1223 impacts; deteriorated reefs are facing severe and widespread loss without active intervention.
1224 - Current efforts aim to extend the natural adaptive capacity of reef-forming coral holobionts
1225 through incorporation of novel tools, methods and environments to manipulate coral adaptive
1226 responses to survive under more extreme or variable conditions.
1227 - Emerging nature-based adaptive approaches spur novel intervention strategies that hold the
1228 promise to be feasible and scalable in the real world but must be tailored to address the diverse
1229 reef, environmental, and ecological conditions.
1230 - Implementing an adaptive intervention framework focused on naturally evolved solutions will
1231 require standardized methodology, appropriate ecological risk-benefit assessments, and
1232 analytical routines for consistent and effective utilization and global coordination.

1233
1234
1235

1236 **Table 1. Approaches to manipulate and harvest the adaptive response of the coral**
 1237 **holobiont.** Deployment-ready indicates whether enough data are available to suggest the
 1238 method works *in situ*, scalability assesses to what extent a method can be scaled up to work at
 1239 the reef dimension. CBASS: Coral Bleaching Automated Stress System

1240

Method	Purpose	Deployment-ready?	Scalability	Costs	Risks	Further Reading
Coral host						
Ex situ spawning system	Offset limitation to rely on natural spawning cycles; for use in coral nurseries	Yes	Low	High	High	50
CBASS	Selection and screening of larvae, colonies and/or genotypes with increased thermotolerance as source material for coral nurseries, coral propagation and/or coral restoration	Yes	High	Low	Low	40
Environmental hardening	Enhance stress tolerance of coral colonies through environmentally mediated priming of stress responses	Yes	Low	High	Low	35,85,239
Selective breeding	Increase frequency of stress tolerance alleles in local populations through selective breeding with resilient genotypes	No	Low	High	High	35,85
Cryopreservation for assisted gene flow	Overcome asynchronous spawning events and assisted gene flow among geographical regions	No	Low	High	High	240-243
Symbiodiniaceae						
Symbiodiniaceae probiotics	Bleaching and mortality mitigation through manipulation of coral symbiont pairings	Yes	Low	High	Low	48
Artificial evolution	Increasing heat tolerance of Symbiodiniaceae through <i>in vitro</i> evolution	No	Moderate	Low	Moderate	126,244
Seeding/exposure of larvae to selected Symbiodiniaceae	Inoculation of early life history coral larvae to manipulate symbiont composition	Yes	Moderate	Moderate	Moderate	138,245
Bacteria						
Use of probiotic consortia	Ameliorate stress and improve coral health (pollution, disease, thermal stress)	Yes	Moderate	Moderate	Moderate	52,246
Use of coral growth promoting probiotics & prebiotics	Accelerate and increase coral growth and calcification in coral nurseries; improvement of coral rehabilitation and restoration efforts through increased survivorship and resilience of fragmented/transplanted colonies	Yes	Moderate	Moderate	Moderate	52
Viruses						
Viral therapy of	Boost stress tolerance	No	Moderate	Moderate	High	186

coral host						
Phage therapy of bacteria	Pathogen control	No	Moderate	Moderate	High	204–207
Phage-BMC combination	Selection of favorable BMC members in addition to pathogen control	No	Moderate	Moderate	High	174

1241

1242 **Figures**

1243

1244 **Figure 1. The coral holobiont (metaorganism).** The holobiont is composed of the coral animal,
1245 obligate intracellular algal symbionts (Symbiodiniaceae), and an assemblage of bacteria and
1246 viruses ¹⁵⁷, among many other organismal entities (such as fungi, endolithic algae, and archaea)
1247 that are less well functionally understood. Viruses putatively intersect all coral holobiont
1248 compartments, can transfer genetic material between holobiont member species, and contribute
1249 to the holobiont's genetic diversity ^{190,196}. Known and inferred functional roles and relationships
1250 between holobiont member species as well as their contribution to metabolic cycling (C, N, P, S)
1251 are depicted. Bold numbers indicate inferred functional roles. Coral holobionts constitute the
1252 foundation (meta)organisms of reef ecosystems, which explains their importance in our efforts to
1253 devise strategies and interventions to save coral reefs.

1254

1255 **Figure 2. Adaptive processes in the coral holobiont and their utilization in adaptive**
1256 **interventions.** Interventions are meant to harness or extend the adaptive capacity of the coral
1257 holobiont to increase their resilience. Note that all adaptive processes, except for evolutionary
1258 adaptation, can happen within the lifetime of the coral holobiont. In the readiness category, the
1259 flask represents successful implementation in lab trials, the coral represents success
1260 implementation in field trials, with brackets denoting approaches that work in principle, but either
1261 standardized and upscaling protocols are needed.

1262

1263 **Figure 3. A scaled adaptive intervention framework.** The development and implementation of
1264 systematic health state surveys can provide a decision-framework with standardized diagnostics,
1265 and, in turn, a suite of indicated intervention measures under consideration of the diverse reef,
1266 environmental, and ecological conditions. The diagnosis of endangered reefs, for instance, could
1267 detail several levels of degradation, where ecological traits such as coral cover, reproductive
1268 potential, and thermal tolerance are differentially affected. Accordingly, degraded reefs could be
1269 defined by pre-dominant presence of bleached and/or diseased colonies that outnumber the
1270 number of healthy colonies. In the scaled adaptive intervention framework, healthy reefs can help
1271 to elucidate the role of coral holobiont entities as targets for adaptive intervention, whereas
1272 endangered and degraded reefs can be targets for a range of manipulative techniques pending
1273 the level of threat and traits to be restored.

1274

1275 **Figure 4. Research roadmap for extending the adaptive capacity of the coral holobiont.**
1276 Emerging approaches (upper half of figure) can inform and integrate with coral restoration
1277 measures (blue arrows). For instance, the thermal stress response of many colonies can be
1278 assessed using a standardized approach (such as the Coral Bleaching Automated Stress System,
1279 CBASS) to identify coral colonies for selective breeding or environmental hardening. In addition,
1280 the success of restoration and/or rehabilitation and probiotic approaches can be monitored with
1281 this system. Likewise, information on genetic diversity can be incorporated into propagation
1282 approaches to enhance thermal resilience and maintain genetic diversity, and *ex situ* spawning
1283 can increase the input of larval supply for coral restoration through propagation. Alongside the
1284 characterization of further holobiont member species with beneficial effects, the study of corals
1285 from extreme environments can inform on and provide a source of adaptive alleles, adaptive

1286 mechanisms, and powerful probiotics underlying coral resilience (lower half of figure). To improve
1287 success and inform adaptive intervention decisions frameworks, it is essential to expand and
1288 integrate knowledge from real world case studies. Increasing standardization and coordination of
1289 efforts can be leveraged through construction of a global database to provide a long-term defined
1290 and coordinated strategy, enable comparative (meta-)analyses, and tracking success to catalyze
1291 and hasten effective coral reef conservation. Standardized, coordinated data recording can serve
1292 as a foundation for building predictive models and analytical frameworks that incorporate
1293 ecological, physiological, and molecular dimensions. Extreme environments image courtesy of
1294 Anna Roik. Mass propagation image courtesy of Jamie Craggs.
1295

1296

1297 **Glossary**

1298

Term	Definition
Acclimation	The physiological process of becoming accustomed to a new condition.
Evolutionary adaptation	The process of genetic change through which individuals of a population become better attuned to their environment
Environmental adaptation	Adaptation is also used more broadly to denote adjustment to prevailing environmental conditions, for example in the context of host microbiome changes
Adaptive capacity	The capacity of coral holobionts to respond to and adjust to environmental stress.
Assisted evolution	Assisted evolution generally refers to human interventions aimed at speeding up natural evolutionary processes to increase the rate of adaptation of threatened species.
Beneficial Microorganisms for Corals	Umbrella term to define (microbial) symbionts that promote coral health; BMCs.
Coral bleaching	Discoloration of coral tissue due to the loss of microalgal symbionts triggered by climate change-induced ocean warming and thermal stress anomalies.
Coral prebiotics	The provisioning of molecules that modulate bacterial (microbial) association to benefit coral host health.
Coral probiotics	The administration of live microorganisms to benefit coral host health.
Environmental hardening	The preconditioning of coral colonies to elevated temperatures as a means to increase tolerance to future heat stress events (can also apply to other stressors).
Environmental rehabilitation	The action of restoring to an improved condition to allow species and ecosystems to thrive under altered environmental conditions.
Restoration	The action of returning something to a former condition, for instance through reinstatement of the original functional or genetic diversity.
Genetically modified organisms	Organisms whose genomes are engineered to produce specific traits of interest; GMOs
Lysis	A common outcome of viral infections, whereby cells are actively induced by viruses to release newly assembled viruses that can then infect other cells.
Microhabitats	A small area that differs from the surrounding habitat, with unique conditions that could select for unique genotypes that might not be found in the remainder of the area.

1299

1300 **TOC summary**

1301 Anthropogenic climate change and environmental deterioration are driving global degradation of
1302 coral reefs. This Review examines how the natural adaptive capacity of coral holobionts can be
1303 harnessed and expanded to counter the ongoing loss of coral reefs.

1304

1305

1306

1307

1308