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Supplementary Materials for

Inheritance of somatic mutations by animal offspring

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Data S1 to S10

Supplementary Notes

Note 1: Chimeras

Coral chimeras harbor two or more diploid genomes. While they have been described in the *Acropora* genus (*71, 72*), they are rare in *A. palmata* (*24*)*.* A previous study characterized only three chimeras (2.2%) out of 90 *A. palmata* genets with at least five ramets (*n*=1,294 samples in total) (*24*). Here, we assessed whether the mutations we observed were due to the parent genet being a chimera. To do so, we must consider the different ways in which chimeras in colonial invertebrates such as corals can form. In integrated chimeras, one of the genotypes may only be present in part of the cells whereas most cells contain the other genotype. For example, chimeric brooding corals can release uniparental, asexual larvae with mixed proportions of the parental genotypes (*73*). In other cases of coral chimeras, portions of the colony may be of one genotype while other portions of the colony may be of a different genotype because of fusion of juvenile recruits. Chimeras developing from broadcast spawners like *A. palmata* are more likely to form due to fusion events of closely related recruits (ie., full or half siblings). The resulting mature colony consists of neighboring groups of polyps from different genets (*60, 72*).

We ruled out the possibility that the parent genet was a chimera for three reasons:

First, a chimera between two siblings or unrelated genets should result in genetic distance values greater than between-ramet values (Fig. 1D and Data S2, (*74*)). The genetic distances among ramets of the parent genet were an order of magnitude lower $(0.0056 \pm 0.0030$ (average \pm SD)) than the genetic distance among full siblings (0.0508 ± 0.0082) and among *A. palmata* genets (0.128 ± 0.025) (Fig. 1D, Data S2 and ref. *26*). On average, the number of probes that differ between siblings is around 1,000, while the maximum number of probes that differed between

the sampled ramets from the parent colony was 52 (Table S1). Therefore, repeated sampling along the two main branches of the parent colony did not reveal evidence of two distinct genets as would be expected from a fusion event of siblings or unrelated recruits.

Second, we reasoned if the parent colony was a fully integrated chimera of siblings at the tissue level, then we would expect differences in the ploidy of the genomic DNA used for the SNP analysis. In humans, chimeras with differing amounts of two genomes have been detected using deviations in the total and relative genotyping array signal (*75*). For our sampled ramets, we did not detect evidence of genome-wide ploidy differences based on the array signal intensity, suggesting they are diploid (see Note 3 below and Data S7).

Third, if the observed mutations were the result of chimerism where the non-mutant somatic tissue is of one genotype and the mutant germline tissue is of another genotype, we would expect all germline variants to be inherited. Instead, only a subset (134 out of 268) were inherited.

Note 2: Detection limits of DNA mixtures

We experimentally tested the ability of the SNP microarray platform to detect when two genotypes are present in one sample, either through contamination or chimerism. Mixtures of extracted DNA from two siblings (pairwise genetic distance $= 0.0709$) were created to represent dominance of one genet (ratios of 85:15, M1) and nearly equal contribution of both genets (ratio of 52:42, M2). The mean nucleotide signals of C or G were significantly higher in the DNA mixtures relative to either Genet A, Genet B, the parental and neighbor ramets or the offspring (1-way ANOVA Tukey *post-hoc*, $p < 0.05$; Fig S3).

Other microarray metrics (heterozygosity, missing data, genetic distance, ploidy differences) were able to detect DNA mixtures when each donor contributed about equal to the mixture (M2) but were not able to detect a minor contribution of a second donor (M1).

Note 3: Mosaicism and Copy Number Variation

Given that each sample represented a non-chimeric mixture of different tissue (e.g., epidermis, gastrodermis) and cell types (e.g., sensory cells, cnidocytes), we sought to determine if the putative SMs were a product of deviations in array signal due to underlying cell mosaicism. Alternatively, array signal deviations could be caused by copy number variations (CNVs) between *A. palmata* and *A. digitifera*, the species used as the reference genome for the analysis, or between the parent genet and offspring samples.

We predicted CNVs using the median normalized log R allele signal intensity estimated for each SNP locus with the R package CGHcall (*66*) and through visual inspection. The log R ratio (LRR) is the relative signal intensity observed for each SNP locus over the expected signal intensity of two genomic copies. Deviations from zero will reflect genomic copy gains (LRR > 0) or losses (LRR < 0). For the *in silico* predictions, we found significantly more CNVs in the offspring (22.1% of all probes) than parent samples (9.3%; $\chi^2(1) = 1213.5$, $p < 0.001$), but no significant difference in the proportion of CNVs that were predicted SMs or inherited SMs between offspring and parents (χ^2 (2) = 0.9703, p= 0.6156; Fig. S5A and B). The CNVs were categorized into double deletion (no allele copies), hemizygous deletion (1 allele copy), normal (2 allele copies), gain (3 allele copies) and amplification (> 3 allele copies). Only hemizygous deletions and gains were detected in the parent and offspring samples, which may represent some level of cell mosaicism in the samples (Data S6). A heat map of CNVs plotted along the longest 1 to shortest scaffolds of the reference genome *A. digitifera* (Fig. S5C) illustrates that some CNVs were recovered in all uniparental offspring (*n*= 50 gain CNVs and *n*=1 loss CNV).

To assess if the *in silico* CNV calls were influenced by the fragmented genome assembly, we 4 visually inspected the log R ratio plots of all predicted SMs (*n*=268, Data S7). Our criteria for visually calling CNVs of the mutant carrying sample were as follows: A) LRR exceeded ± 0.5 and the BAF \sim 0.5 (double deletion), B) LRR exceeded \pm 0.5 and the BAF = 0.4 or 0.6 (single deletion), and C) LRR exceeded \pm 0.5 and the BAF = 0, 0.33, 0.67, or 1 (duplication: AAA, AAB, ABB, BBB, respectively) (*76, 77*). There were 95 SMs detected as a CNV by at least one method and 14 shared by both methods (Fig. S5E). No difference in copy number was detected in the remaining 173 SMs (Fig. S5E), of which 82 were inherited SMs (example in Fig. S6, Data 1 S6). The CNVs detected were a fraction (39%) of the inherited SMs.

Note 4: RFLP validation of SMs 3

Ten SNP-containing regions were amplified by PCR, and the resulting PCR product was digested by a restriction enzyme (Fig. 1C and Data S8). Two loci were detected to have some copy number variation and eight were without copy number variation (see Note 3). Markers that produced both sharp PCR bands and clear results in restriction digests were further investigated (*n*=2 markers out of 10). Of these markers, GOH variant mutation locus AX-212313644 produced the clearest banding patterns on gels. Two offspring (SWSA-179, SWSA-181), share the heterozygous mutation with the parent 453, resulting in 3 bands (Fig. 1C) while parent 455 predicted to have the non-mutant homozygous state for this site did not cut, resulting in 1 band (Fig. 1C).

The copy-number variant, AX-212294854, was also confirmed through this method (Fig. S7). The mutant allele for this probe was heterozygous, so that the expected banding pattern was three bands. The major allele for this probe was homozygous for the allele not recognized by the restriction enzyme, and therefore was expected to not be cut. There was significant observed STAR activity in this probe (more fragments than expected by the individual cut site). This could be explained by the observed copy number variation between the offspring and parent that share the heterozygous mutation (Data S6), resulting in the excess bands seen in Fig. S7. The RFLP marker confirms the inheritance of the GOH mutation found at this locus discovered in the SNP array data.

Not all identified mutations with designed assays were validated with this method. For the mutation of probe AX-197939655, the major allele shared by most samples was homozygous for the allele not recognized by the enzyme, and the mutant was heterozygous at that restriction site. The restriction enzyme did not cut the PCR product of the mutant offspring for this restriction site, suggesting that the mutant site was homozygous contrary to expectations.

Note 5: Somatic mutation detected in Florida larvae

The first indication that somatic mutations could be passed to offspring came from a 2017 observation where we detected known somatic mutations in microsatellite loci from offspring of two *A. palmata* genets from Florida (*24*). Most larvae (61.3%, *n*=39) were produced with genetic contributions from both parents, but 38.7% (*n*=24) contained genetic contributions from only one parent (uniparental larvae) (Data S10). It was unclear whether these offspring were the product of self-fertilization or parthenogenesis, but either way indicated that *A. palmata* colonies employ a wider range of reproductive modes than previously thought (*38, 54*). Somatic mutations were

detected in six uniparental larvae and one biparental larva (Fig. S7)*.* The six uniparental larvae appeared to be diploid because they inherited two different alleles at one or more loci that were heterozygous in the parent.

Fig. S1. Summary of reproductive strategies of broadcast spawning corals. (A) *A. palmata* gametes are mostly self-incompatible so that fertilization occurs only between gametes from different genets (biparental outcross)**.** However, self-fertilization and parthenogenic offspring were observed in this study. **(B)** Overview of the genetic consequences of the different reproductive modes on ploidy (n) and heterozygosity.

Fig. S2. SNP microarray performance on DNA mixtures of two genets. (A) Samples from *A. palmata* colonies are dominated by somatic tissue (orange). Germline tissue is restricted to mesenteries where gametes are produced (blue, inset) (*78*). The red star denotes the occurrence of a somatic mutation that has been fixed within a polyp. A DNA sample typically consists of 3- 4 polyps mostly composed of somatic tissue. **(B)** Mixtures of DNA extracted from two siblings, Genet A and B, were created to represent dominance of one genet (ratio of 85:15, M1) and nearly equal contribution of both genets (ratio of 52:42, M2). **(C)** Mean signal intensities for each nucleotide (A, T, C and G) by group. Statistical differences from a Tukey *post hoc* test following a 1-way ANOVA are indicated by differing lowercase letters. The artificial DNA mixtures, M1 and M2 (M1: $n=1$, light purple and M2: $n=1$, dark purple) resulted in higher signal means than signal means from samples of the donor genets A and B (*n*=4, orange), the samples from the neighbor colonies (*n*=5, gray), the samples from the parent colony (*n*=10, black) or the uniparental offspring (*n*=30, blue).

Fig. S4. Deviations in array signal indicate potential copy number variation. (A) UpSet plot of loss (blue) or gain (orange) copy number variants (CNV) detected *in silico* for two groups, offspring (*n*=30) and parents (*n*=15). The horizontal bar plots show the total number of loci with *in silico* detected CNVs for each group. The asterisk indicates significance from a chi-square test, alpha level = 0.05. The vertical stacked bar plots show the number of shared CNVs for each group. Each bar is split by the proportion of non-mutant (grey), somatic mutations (SMs, dark blue) and inherited SMs (light blue). The connected colored circles below the plot show groups that share the number of CNVs indicated by the above bar. **(B)** The top right inset plot is the proportion of shared CNVs for the SMs only (SMs: dark blue; inherited SMs: light blue). **(C)** A heat map of the *in silico* detected CNVs for each sample along the *A. digitifera* scaffolds. **(D)** Venn diagram of the SMs detected as CNVs (*n*=95) from *in silico* and visual inspection of the log R ratio plots (Data S8). The remaining SMs (*n*=173) were not predicted to be CNVs by either approach.

Fig. S5. An example of copy number variation of an inherited SM. B-allele frequency (top) and log R ratio (bottom) for the fifteen parent and thirty offspring samples for locus AX-212309463. The blue panel labels are those samples that share a predicted loss of heterozygosity SM and orange labels are those samples that share a gain of heterozygosity due to CNV.

Fig. S6. Inherited GOH mutation locus AX-212294854. (A) B-allele frequency and log R ratio of parent 3 and offspring 126 with a shared heterozygous mutation while other parent and offspring samples share the non-mutant homozygous state. The log R ratio of the parent and offspring sample that shared the mutation exceeded the 0.5 threshold for copy number changes, suggestive of a CNV at this locus. **(B)** RFLP validation of AX-212294854. For each sample, the uncut (U) and cut (C) PCR products are shown. Each gel contains a size standard (lane M, bp = base pairs). The heterozygous mutation resulted in the three predicted bands in the offspring 126 and parent 3, as well as several others presumably due to CNVs.

Fig. S7.

Fig.S7. Examples of inheritance of somatic mutations detected with microsatellites. Four distinct patterns of allelic inheritance were observed across five *Acropora*-specific microsatellite loci. Examples of these four patterns (L1, L2, L3 and L4) are depicted here. Gametes were collected from two hermaphroditic *A. palmata* colonies (P1 and P2) that each had known somatic mutations in one of the five loci assayed (166, 181, 182, 192, 207). Ancestral alleles are indicated by solid-colored blocks, mutated alleles are indicated by blocks with vertical black lines. While diploid in the ancestral state (represented as two blocks per locus), *A. palmata* ramets can gain alleles over time via gene duplication (three blocks per locus (*24*)). P1 and P2 were crossed. Allelic patterns in most resulting biparental larvae (larval cohort L1) followed Mendelian expectations (60.3%) while only one biparental larva, L2, was observed to have mutated allele. A subset of larvae (cohorts L3 and L4) was uniparental in origin. Larvae in cohorts L3 and L4 inherited alleles from only one parent (P2), including the somatic mutation at locus 166 in the L3 cohort. Note that L4 larvae could either be haploid or diploid.

Table S1. *A. palmata* **samples analyzed by the SNP array.** Group refers to the parental samples or offspring analyzed (Fig 1A). The affymetrix ID is the unique sample identification number and the coral multi-locus genotype identification (MLG ID) is the unique genet identification number from the STAGdb (*26*). The grey shaded MLG IDs were identified as the same genet. Percent missing data and heterozygosity were calculated from 19,696 genotyping SNPs. The number of SMs were tallied from the minority SNP allele calls of the parental genet and those shared by the offspring.

Table S2. Number of mutations shared by samples of the parental genet. SNPs shared by seven or fewer samples were considered to be somatic mutations.

Data S1. Absolute genetic distance matrix between parents and uniparental offspring. (Excel Workbook)

Data S2. Somatic mutation alleles identified in SNP array samples. (Excel Workbook)

Data S3. Count of transitions, transversions, gains and loss of heterozygosity. (Excel Workbook)

Data S4. Predicted variant effects for the putative somatic mutations. (Excel Workbook)

Data S5. Mutations unique to uniparental offspring. For each probe (column 1), the offspring genotype in 0 and 1s is presented. The last two columns provide the scaffold ID and position for the SNP probe. (Excel Workbook)

Data S6. Frequency of parent genet or offspring with predicted gain or loss CNVs for each locus. (Excel Workbook)

Data S7. BAF and LRR plots for mutation-containing *A. digitifera* scaffolds (PDF)

Data S8. Restriction fragment length polymorphism design for 10 probes with putative inherited mutations. (Excel Workbook)

Data S9. Putative somatic mutations of the Curacao parental genet in the biparental offspring. The alleles of the Curacao genet mutations (*n*=268) were tracked through the Curacao x Florida biparental offspring (*n*=11) by comparing the observed versus expected proportion of alleles for the ancestral allele of both parent genets. Probes where observed allele frequencies match expected frequencies for the ancestral allele are colored white. Probes where the allele frequencies observed do not match expectations of the ancestral allele but could arise from the mutant allele are colored blue. Probes where allele frequencies observed do not match expectations of the ancestral or mutant alleles, but could arise from other sources (germline mutations, non-Mendelian inheritance, somatic mutation post-fertilization, or genotyping error) are colored orange. (Excel Workbook)

Data S10. Parental and offspring microsatellite allele sizes. Two copies of the same allele size are indicated by a slash $($). Reproduction status is inferred from the allele copies for each individual. The different observed alleles are denoted as a1 to a*n* for each microsatellite marker, where n is the total number of unique alleles present. (Excel Workbook)

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