UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

INTEGRATED DNA TECHNOLOGIES, INC.,
Petitioner,

v.

TECAN GENOMICS, INC.,
Patent Owner

Case IPR2025-00015
Case IPR2025-00016
U.S. Patent Nos. 10,036,012 and 10,876,108

DECLARATION OF MIKHAIL V. MATZ, PH.D.

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I, Mikhail V. Matz, declare as follows:

1. I have been retained by Patent Owner, Tecan Genomics, Inc. ("Tecan") to provide testimony in this *inter partes* review regarding my work with early NGS techniques.

2. I am the senior author of the research article *Sequencing and de novo analysis of a coral larval transcriptome using 454 GSFlx*, which I understand to be referred to as Meyer, Meyer 2009, or EX1006 in this proceeding. This work was performed in my lab under my direction.

3. Tecan requested that I submit this declaration to aid the Patent Office in its review of Meyer.

4. I understand that there are two *inter partes* review proceedings concerning my work and that IDT relies on my work for its anticipation and obviousness arguments. I have not been asked to provide any opinions as to the ultimate issues of anticipation and obviousness that IDT has raised.

I. BACKGROUND AND QUALIFICATIONS

5. Over the past three decades, I have studied and researched various topics in biochemistry and marine biology, including methods for PCR amplification, PCR suppression, and coral genomics.

6. I obtained my Ph.D. in Biochemistry in 1999 from the Institute of Bioorganic Chemistry in Moscow, Russia. As part of my graduate studies in

Moscow, I researched and published on molecular cloning, cDNA normalization, PCR suppression, and PCR amplification.

7. I conducted my postdoctoral studies in the Whitney Laboratory for Marine Bioscience at the University of Florida, St. Augustine, from October 2000 to May 2001. Afterwards, I became a research assistant professor in the Whitney Lab. I also held a joint appointment as an assistant scientist in the Department of Molecular Genetics and Microbiology at the University of Florida. I held these appointments from May 2001 to August 2006.

8. In August 2006, I joined the University of Texas at Austin as an Assistant Professor in the Integrative Biology section. I have remained at this institution for the past 18 years. I am currently at the rank of tenured full Professor, since August 2019. As part of my responsibilities as an Assistant Professor and now tenured full Professor, I serve as the principal investigator for a genomics research laboratory. As the principal investigator, I oversee the research conducted in the laboratory, including the work described in Meyer. During this time, I have published 95 peer-reviewed papers on coral genomics, transcriptomics, and epigenetics. My research has been referenced in published works of others more than 23,000 times, currently accumulating about 1,500-1,600 new references per year.

9. I understand that one of these publications on sequencing and coral genomics, Meyer, is at issue in these proceedings. We conducted the study described in Meyer in 2008 and submitted it for publication on January 13, 2009. I led the team that developed the methods that were used and oversaw the experiments and analysis that were done. I also helped draft and edit the Meyer manuscript prior to its publication in 2009.

10. Meyer represents a culmination of work between my laboratory, the Center for Genomics and Bioinformatics at Indiana University, and James Cook University in Australia. My laboratory prepared the sequencing library used in Meyer while researchers at James Cook University facilitated sample collection, and researchers at Indiana University sequenced the library with the 454 sequencer. EX1006.0017.

11. I conceived of the study and library preparation methods described in Meyer. *Id.* Postdoctoral researcher Eli Meyer and research assistant Galina Aglyamova helped prepare the cDNA sequencing library used in Meyer. *Id.* Another postdoctoral researcher, Shi Wang, analyzed single nucleotide polymorphisms ("SNPs") in the sequencing data and validated the results. *Id.* I supervised their work.

12. A copy of my curriculum vitae, attached as **Exhibit A**, contains further details on my education, experience, publications, and the other qualifications allowing me to render an opinion in this matter.

13. I am being compensated my standard rate of $250 per hour, plus expenses. My compensation is in no way dependent on the content of my testimony or upon the outcome of this proceeding.

14. I have not previously testified as an expert witness.

II. THE STUDY IN MEYER FOCUSED ON SEQUENCING THE ENTIRE CORAL TRANSCRIPTOME IN ONE SEQUENCING RUN

15. In 2008, my lab focused on studying various species of coral and their role in sustaining marine ecosystems. We were interested in understanding the stress tolerance of coral and the interactions between coral and algae—both issues that were poorly understood at the time. This was important to us because it could help us better understand what impact climate change and other environmental stressors would have on marine ecosystems. By 2008, we recognized an urgent need to understand the potential for corals to adapt to climate change. *See* EX1006.0001-02.

16. As we reported in our publication, we felt that new methods were needed for "genomic-scale analysis of emerging model organisms that exemplify important biological questions but lack fully sequenced genomes." *Id.*, .0001. We believed that NGS could be harnessed to "make possible the detailed studies of gene

expression, genetic connectivity, and stress physiology required for addressing" the questions being investigated by my lab. *Id.*, .0002.

17. While a few studies had already used NGS technology to sequence the transcriptomes for organisms with already completed genomes, we observed a lack of methods for *de novo* assembly and analysis of transcriptomes without a reference genome sequence, which limited the study of emerging model organisms. *Id.* Even more, we noticed that NGS methods had not yet been applied to corals. *Id.* In fact, only a small set of sequencing reads were available for just three coral species. *Id.* Some studies had used Sanger sequencing to identify expressed sequence tags (short sequences that correspond to expressed genes) and partial genome sequences. *Id.* But no coral genome or transcriptome had been completely sequenced and assembled. *See id.*

18. We wanted to facilitate genomics studies in corals and other non-model systems through the use of NGS technologies given their increased throughput, which could expand the amount of known sequencing data. *Id.* NGS was not widespread at the time since it had only been commercially available for a few years. Moreover, in these early days of NGS, researchers had just begun to adapt the technology to their respective disciplines. At the time, the 454 pyrosequencer had been commercially available for about three years, and the Solexa Genome Analyzer

(what would later be acquired by Illumina) had been available for about two years. The Ion Torrent sequencer would not be released for over another year.

19. Not only was NGS relatively new, but researchers were also concerned with the accuracy of the platforms available. While NGS made it possible to sequence considerably larger volumes of genetic material more efficiently, NGS suffered from a number of problems that resulted in lower quality sequencing reads than Sanger sequencing. These concerns were exacerbated when there was no existing reference genome since researchers had no way of comparing to see whether the sequencing reads were inaccurate.

20. Through Meyer, we wanted to demonstrate as a proof of concept that researchers could deep sequence entire transcriptomes of emerging model organisms in a single 454 sequencing run and rely on that sequencing data to *de novo* assemble entire transcriptomes. *See* EX1006.0002. Our improvements to existing methods focused on ways to improve sequencing read output and to assemble catalogs of genes from that output. *Id.* To demonstrate the effectiveness of our improvements, we applied these methods to sequence the larval transcriptome of the coral *Acropora millepora*. *Id.*

21. As we report in Meyer, we succeeded in sequencing the entire transcriptome. *Id.*, .0001. I believe this was one of the earliest instances in which a lab had succeeded in fully sequencing a transcriptome of a non-model organism with

no prior genomic resources, using the 454 sequencing platform. Our study also succeeded in assembling and annotating the transcriptome of the *A. millepora*, which provided critical insight into the genetic makeup of the coral species, furthering other coral research.

III. HOW WE OVERCAME CHALLENGES TO SEQUENCE AN ENTIRE TRANSCRIPTOME

22. The sequencing results reported in Meyer were generated with the 454 GS-Flx sequencing platform. EX1006.0001. Our primary goal in Meyer was to sequence the entire transcriptome. *See id.* This meant that our biggest challenge would be to ***avoid the preferential sequencing of certain genes or transcript regions*** and to ensure that the whole transcriptome was covered as evenly as possible. This required overcoming biases towards highly abundant transcripts, the 3' ends of transcripts, and shorter transcripts. The second challenge would be to avoid sequencing our own artificial adaptors so that we could maximize the output of actual new coral sequences. The third challenge would be to mitigate 454-specific optical artifacts stemming from the sequencing of the poly-A tails that are present at the 3'-end of every transcript.

A. Overcoming Bias Towards Highly Abundant Transcripts

23. Transcript abundances can vary by several orders of magnitude across genes. If such a sample were to be sequenced directly, we would have enormous sequencing coverage for a small number of genes producing highly abundant

transcripts, while the rest of the transcriptome would get little or no coverage. To solve this problem, we applied the normalization procedure implemented in the Evrogen Trimmer kit. *See* EX1006.0013; EX2081. This procedure equalizes the abundances of transcripts, reducing the difference in their relative representation from several orders of magnitude to just 2-3 fold, reducing the problem dramatically. In Meyer, we applied this normalization procedure after cDNA synthesis and before fragmentation. *Id.*

B. Overcoming Bias Towards 3'-ends of Transcripts

24. In the protocol for cDNA synthesis that we used in Meyer, the cDNA synthesis is initiated using an oligo-dT containing primer, which anneals to the poly-A tail present at the 3'-end of every protein-coding RNA. *Id.* This method of cDNA synthesis was introduced in the 1990s and has an important advantage of selecting against ribosomal RNA, which is of no interest to us but constituted over 90% of the sample.

25. The RNA molecule was then copied by the reverse transcriptase (RT) enzyme into cDNA, going from the 3' to 5' ends of the mRNA. Sometimes, the RT enzyme failed to copy the entire length of the RNA molecule. This was especially more likely to occur the longer the RNA molecule was because the RT enzyme would need to copy more nucleic acids. *See* EX1034.0004. This premature termination of the copying process could lead to over-representation of 3' regions since the copying

process begins at the 3' end. *Id.* In these instances, the 5' end of the RNA molecule would be under-represented in the cDNA copies. *Id.* To avoid the 3' over-representation (and 5' under-representation), we used the SMART cDNA amplification kit (Takara). EX1006.0013. This kit uses a "template-switching" method to amplify RNA molecules that have been copied in their entirety. As such, we were able to ensure that the cDNA copies contained the 5' and 3' ends as well as the nucleic acid sequences in between.

C. Overcoming Bias Towards Shorter Transcripts

26. Polymerase chain reaction ("PCR") amplification has a well-known tendency to increase the representation of shorter molecules in a mixed sample (such as a transcriptome library), because shorter fragments are amplified more efficiently. *See* EX2081.0009. To combat this tendency during our library preparation procedure, we normalized and amplified the original cDNA library with primers annealing at both ends of each fragment (as per the SMART cDNA amplification protocol). EX1006.0013. We also used a low number of PCR cycles (15) to amplify the normalized library, which reduced the chance for PCR artifacts to accumulate. *Id.*

D. Avoiding Non-Productive Sequencing of Artificial Adaptors

27. If we were to simply take our normalized cDNA sample and use the standard 454 sequencing library preparation kit on it, as much as one-quarter of all

reads would have been unusable, containing mostly or exclusively sequences of adaptors used during the library preparation. To avoid this, we developed the sequencing library preparation scheme that avoids placing the read-initiating primer next to adaptor sequences. This scheme is outlined in Figure 1 below:

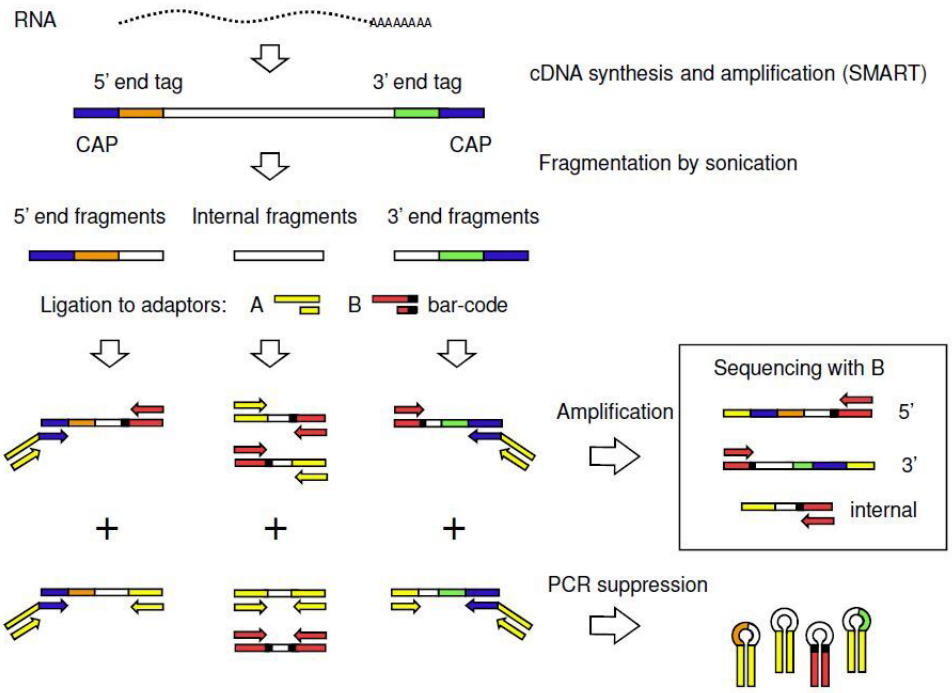


Figure 1
Diagram of cDNA synthesis and 454 library preparation procedures. Three fragment types are produced by sonication: 5', internal, and 3'. Ligation with the partially double-stranded adaptors A and B produces, for each fragment type, certain adaptor configurations that will be amplified (above the '+'), and others that will be suppressed (below the '+') during the subsequent amplification. The procedure preferentially amplifies constructs that are appropriate for 454 sequencing (shown inside box).

EX1006.0003. The read-initiating primer, shown as a red arrow in the figure, always points towards the white part of the DNA, which is the original coral transcript sequence, and is not located next to the adaptors. An additional feature of this scheme is the suppression of amplification for unsequenceable fragments flanked by the same primer on both ends (what we refer to as PCR suppression in Meyer). *Id.*

E. Avoiding "Blinding" the 454 sequencer with Poly-A Tails

28. The 454 sequencer used pyrosequencing by creating DNA complementary to the fragments to be sequenced. This process featured rounds of controlled nucleotide incorporation where the sequencing plate was washed with only one nucleotide species (e.g., A, T, G, C) for any given round. Each incorporation would emit light because of the pyrophosphate released during the reaction. Optical sensors in the 454 sequencer would detect these light emissions for each fragment being sequenced and generate graphs that could be used to identify sequences.

29. In a typical nucleotide sequence where the sequence is varied, a single nucleotide would be added to the complementary sequence, emitting a single signal pulse. However, when several bases of the same kind appear in a row (a homopolymer comprising, for example, sequences CCCC or AAAAAA), the addition of the homopolymer-forming nucleotide in that round results in multiple base incorporations, generating a brighter light signal. The brightness of this signal is used by the 454 instrument to infer how many bases are repeated within the homopolymer sequence.

30. This method can malfunction with the poly-A sequence found at the end of every protein-coding transcript. Assuming a typical library preparation protocol (such as the SMART cDNA amplification kit), the poly-A tail could be 30

bases long. Incorporation of that many nucleotides in the same 454 sequencing round would generate a far stronger burst of light than the 454 platform's sensors were equipped to handle. Such a burst would essentially blind the sensors, throwing off their calibration and leading the instrument to discard the whole read as well as reads in neighboring microwells, which could result in the failure of the whole sequencing run.

31. Even though we ensured that sequencing always starts from the actual coral transcript part (Figure 1), due to the randomness of fragmentation, the coral part can be short enough for the read to run into the adaptor sequence, including the poly-A/T stretch. Even though we used a shorter poly-T-primer than standard (with only 13 "T" bases in a row, *see* EX1006.0013), any sequencing of that region would have led to us having to discard the poly-A/T containing reads and nearby wells. To fix this, we introduced an additional modification: a "broken-T" primer, where we interrupted the T(13) homopolymer with a single "C" base in the middle. *Id.* We did this to avoid the "sensor-blinding" problem with the 454 sequencer.

IV. OUR METHOD IN DETAIL

32. There are two library preparation methods reported in Meyer: the method illustrated in Figure 1 and the method illustrated in Additional File 4. As we reported in the publication, we only used the method reported in Figure 1 to prepare the samples that were sequenced and reported in Meyer. EX1006.0002 ("A cDNA

sample was prepared from coral larvae as illustrated in Figure 1"). Unless otherwise specified, any references I make to the method reported in Meyer refer to the method reported in Figure 1.

33. The method incorporates the solutions outlined above and was used to prepare the mRNA transcripts for sequencing. Figure 1 is an accurate representation of cDNA synthesis and library preparation in the method.

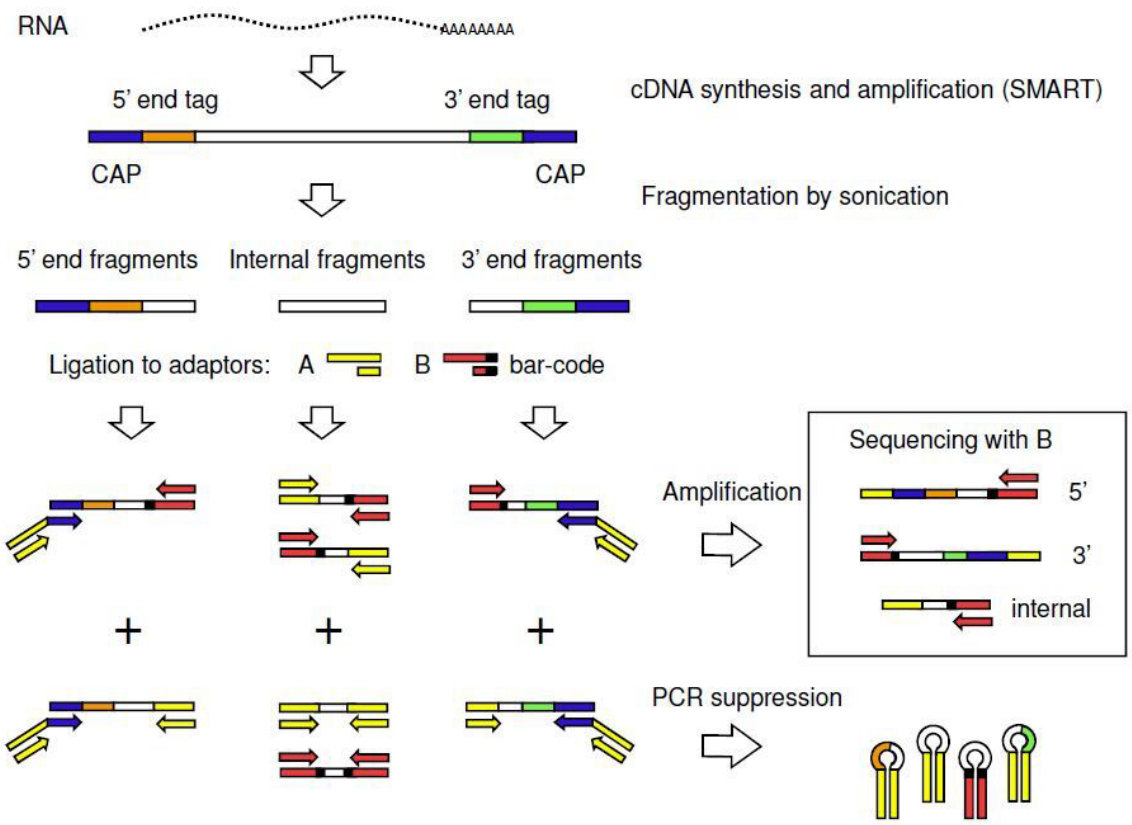


Figure 1
Diagram of cDNA synthesis and 454 library preparation procedures. Three fragment types are produced by sonication: 5', internal, and 3'. Ligation with the partially double-stranded adaptors A and B produces, for each fragment type, certain adaptor configurations that will be amplified (above the '+'), and others that will be suppressed (below the '+') during the subsequent amplification. The procedure preferentially amplifies constructs that are appropriate for 454 sequencing (shown inside box).

34. In our study, we extracted RNA from coral larvae using a standard extraction kit. *Id.*, .0012. We purified the extracted RNA through lithium chloride precipitation, which removes contaminating DNA and proteins. *Id.*, .0012-13. The precipitant was centrifuged and analyzed on a gel to ensure purity. *Id.*, .0021.

35. 454 sequencing required that the RNA be converted to cDNA before the nucleic acids could be sequenced. We used Clontech's SMART cDNA synthesis and amplification kit to reverse transcribe and amplify purified RNA. *Id.*, .0012. This was a standard procedure at the time. We also used this kit because it is designed to only amplify cDNAs that have been reverse-transcribed in their entirety, "preferentially enrich[ing] for full-length cDNAs." EX1034.0004.

36. We followed the manufacturer's instructions for cDNA synthesis, except that the primer used for the first strand of cDNA synthesis was customized to incorporate the broken chain T sequence. We did this "by the inclusion of an internal C to minimize the potential for 454 sequencing problems in [the] homopolymer stretch." EX1006.0013. The modified CAP primer with the broken chain is shown below.

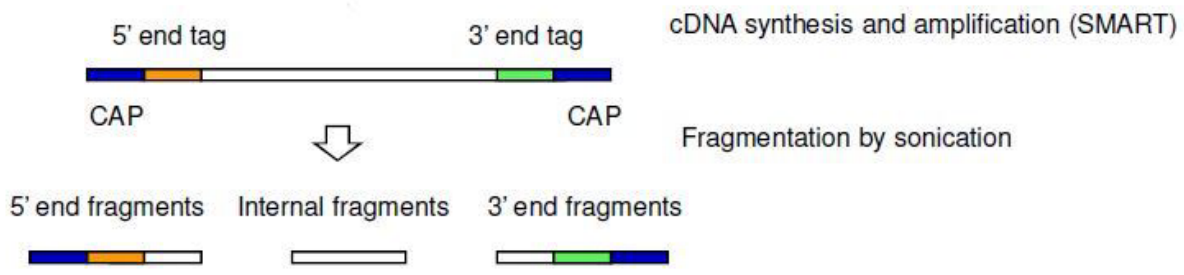
Cap-TRSA-CV (first strand cDNA synthesis primer):
5'- AAGCAGTGGTATCAACGCAGAGT CGCAGTCGGTACTTTTTTCTTTTTTV – 3'
("cap" primer sequence) ("broken chain" polyT)

Id., .0019.

37. The SMART protocol amplifies the cDNA strands by using the CAP primers. We followed the manufacturer's instructions and used PCR suppression to "preferentially amplify longer molecules and thus enrich for full-length transcripts." *Id.*, .0013. This preferential amplification was important because it counteracts the natural tendency of PCR to amplify shorter molecules over longer ones, which would have created a bias towards shorter transcripts. EX2081.0009. This entire process occurred before fragmentation. *See* EX1006.0013, .0021-23.

38. After we normalized and amplified the full-length cDNA strands, we fragmented them by sonication to produce short, random fragments appropriate for 454 sequencing. *Id.* We optimized this process to produce fragments that were roughly 300-400 nucleotides in length. *Id.*, .0013.

39. As depicted in Figure 1, fragmentation generated three types of fragments: (1) internal fragments that represented most of the regions of the mRNA transcripts; (2) 5' end fragments; and (3) 3' end fragments.



EX1006.0003. The above figure is a simplification of the process and does not reflect the ratio of fragment types. For every pair of end fragments, there were

several internal fragments. Altogether, these fragments represented the entire length of the cDNA strand. The end fragments retained the CAP primers at their termini (shown in blue above). The 5' and 3' end fragments contained slightly different CAP primers with the 3' end fragment CAP primer incorporating the broken chain T sequence (shown in green above).

40. We ligated pseudo-double-stranded adaptors that either contained the Primer A or Primer B sequence to polished cDNA fragments. *Id.*, .0013. These adaptors are illustrated below.

B+ adapter:
Long oligo: 5'-GCCTTGCCAGCCCGCTCAG ACGAGCGGCCA-3'
(B primer sequence) (suppression tag)
Short oligo: 5'-TGGCCGCTCGT-3'

A+ adapter:
Long oligo: 5'-GCCTCCCTCGCGCCATCAG CCGCGCAGGT-3'
(A primer sequence) (suppression tag)
Short oligo: 5'-ACCTGCGCGG-3'

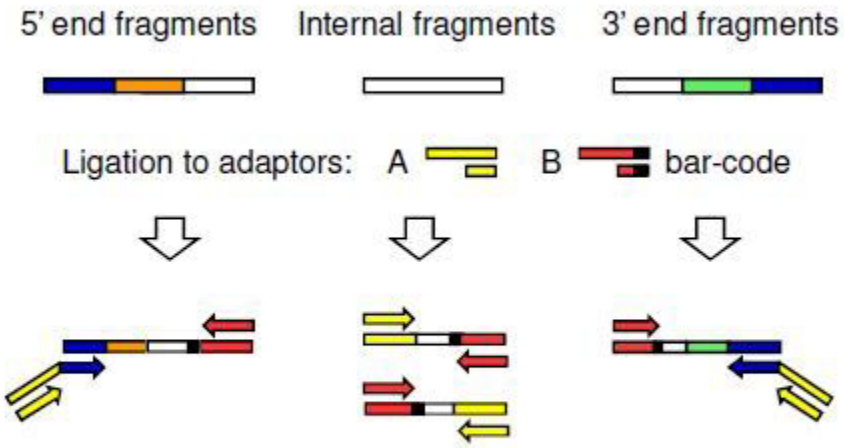
EX1006.0019. As reflected in the illustration, each adaptor contained suppression tags.

41. These adaptors were only ligated to the "new" 5' ends formed as a result of fragmentation/polishing. *Id.* Since the incorporated CAP primer used for cDNA amplification was present on the original ends of the cDNA strands and lacked 5' phosphates, the pseudo-double-stranded adaptors were not able to ligate to them. *Id.* At the initiation of PCR amplification (before the first DNA denaturation step), the

DNA polymerase in the reaction would fill in the primer binding sites on complementary strands.

42. We then annealed the universal primers A and B and a primer known as "A+CAP" to the fragments. *Id.*, .0013. The "A+CAP" primer was complementary to the CAP primer sequences and contained the Primer A sequence at one end of the primer. *Id.* The "A+CAP" primer was used to incorporate the "A+" sequence at each of the original cDNA termini. *Id.*, .0019. This was important because without it, the end fragments could not be attached to the 454 beads for sequencing.

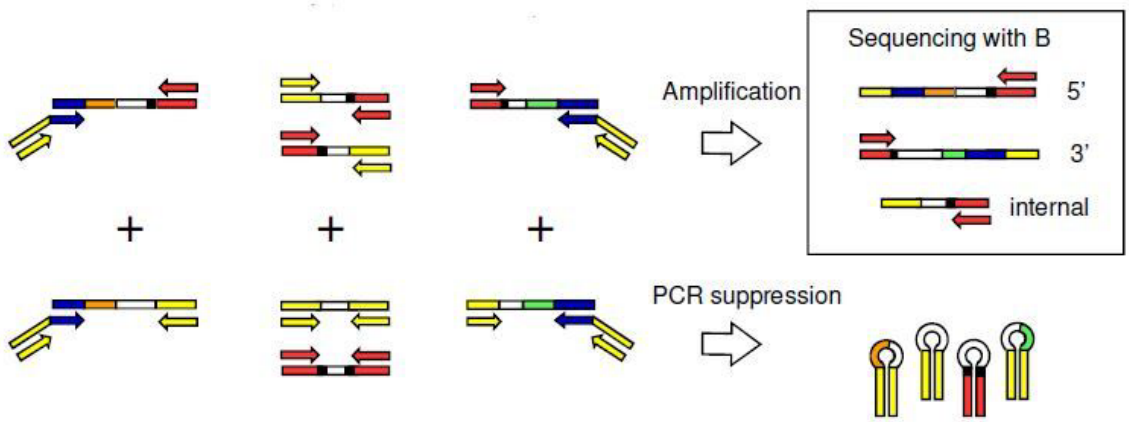
43. The A, B, and "A+CAP" primers were all added to the mixture after adaptor ligation and before annealing. *Id.*, .0013. The directed ligation of the pseudo-double-stranded adaptors and annealing steps are illustrated below.



Id., .0003. The CAP primers (blue) are attached to the two termini of the original cDNA strand. The pseudo-double-stranded adaptors ligate to the uncapped ends of the cDNA fragments (white). The "A+CAP" primers (blue arrows) anneal to the CAP primer sequences. The "A+CAP" primers contain the Primer A sequence (yellow) at their ends.

44. After the primers anneal to their corresponding sequences on the fragments, extension products are generated. For the end fragments, these extension products incorporate the Primer A sequence. Because Primers A and B are also present in the mixture, extension products are generated for the internal fragments as well.

45. Amplification then proceeds using Primers A and B. All fragments with a Primer A binding site on one end and a Primer B binding site on the other end were exponentially amplified. Any fragments with matching primer binding sites (i.e., two Primer A or two Primer B binding sites on the same fragment) were suppressed through PCR suppression and not exponentially amplified. The PCR suppression and amplification steps are illustrated below.

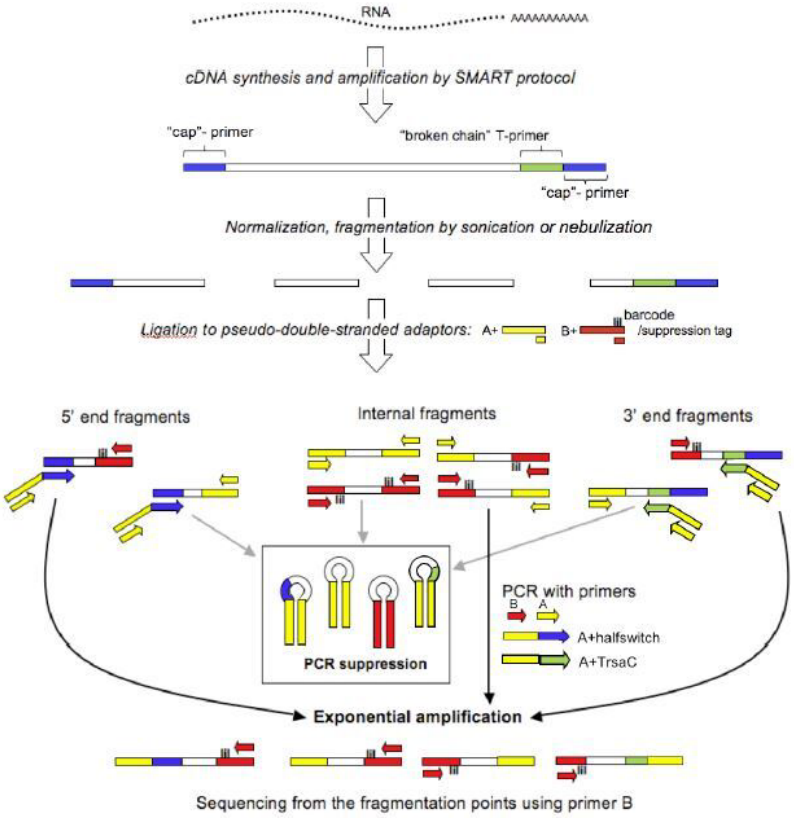


Id., .0003. The top row of fragments reflects the configurations where exponential amplification proceeded. Each fragment only contains one Primer A sequence and one Primer B sequence. The bottom row of fragments contain either two Primer A sequences or two Primer B sequences. These fragments formed hairpins and were not amplified. The box in the top right of the figure shows the configuration of the three types of sequences that were amplified and sequenced. As illustrated in the figure, amplification occurred for all fragments with the proper adaptor arrangement, and PCR suppression occurred with all fragments having two copies of the same adaptor. Because the two types of pseudo-double-stranded adaptors were ligated randomly to all non-capped fragment ends, both end and internal fragments were PCR suppressed.

46. After additional purification steps, we sequenced the fragments using the 454 GS-Flx platform. *Id.*, .0014.

47. As I noted above, we also reported an "improved protocol" that included "minor modifications that we ha[d] recently developed to reduce the number of manipulations required, improve reproducibility, and to further reduce adaptor concatenation." *Id.* As we noted in Additional File 4, the minor modifications were to the process for "preparing coral larval cDNA." *Id.*, .0019.

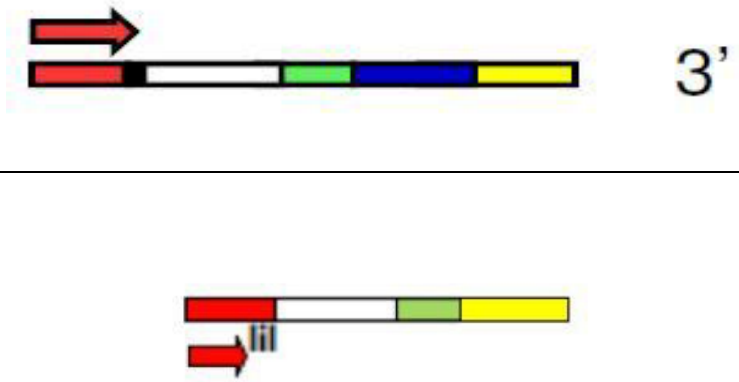
48. The below figure is an accurate representation of this modified method and reflects the changes made to the library preparation method:



49. In the modified method, we introduced a fourth primer, the "A+TrsaC" primer. This primer contains a sequence complementary to the broken T chain rather than the CAP primer. This primer is illustrated below.

A+TRSAC:
5'-GCCTCCCTCGCGCCATCAG CCGCGCAGGT CGCAGTCGGTACTTTTTTCTTTTTT
(A primer sequence) (suppression tag) (sequence of the 3'-portion of the "broken chain" cDNA synthesis primer)

Id., .0019. We suggested using this primer because it reduces the length of the subsequent amplicons, which now no longer contain the CAP primer sequence. I have included below an illustration comparing the composition of the amplicon generated from the general method to the amplicon generated from the modified method.



50. As shown by the figure, the CAP primer sequence (which is 23 nucleotides in length, *see* EX1006.0019) is no longer present in the amplicons generated by the modified method. By reducing the read length of the 3' end

fragment further, we could reduce the risk for sequencing errors. We also could conserve space, meaning that more of our sequencing reads were directed to genetic material from the sample and not to adaptors. While that may seem trivial when considering a single fragment, it is not so trivial when sequencing over 600,000 fragments, where this simple fix can reduce the number of nucleotides sequenced by 13.8 million.

V. OUR RESULTS

A. Assembling a Full Larval Transcriptome of *Acropora millepora*

51. Our goal was to demonstrate that it was possible to sequence the entire transcriptome in one sequencing run using our method. From the method, we produced 628,649 raw sequencing reads from a single sequencing run. EX1006.0002. These raw reads correspond to the number of sequencing reads that we received back from the 454 sequencer before we performed any further quality controls.

52. To verify that we were able to sequence the entire transcriptome, we needed to use those reads to assemble the transcriptome. After we trimmed the adaptors from the reads and normalized for size (i.e. size selection), we were able to assemble 44,444 contigs. *Id.*, .0003. A contig is a continuous stretch of overlapping sequencing reads. If we think of a single sequencing read as one piece of a jigsaw puzzle, a contig may be thought of as four or five pieces that fit together.

53. After assembly of the contigs, we were left with 62,657 singletons. *Id.* A singleton is a single sequencing read that cannot be joined to form a contig. While singletons may be unique portions of the transcriptome that do not overlap with other sequencing reads, singletons may also represent sequencing errors, artifacts of cDNA normalization, or contaminants from other sources. Our analysis of the singletons showed that "a substantial fraction" were in fact "artifacts of cDNA synthesis, normalization, or sequencing." *Id.*, .0010. These singletons would be the equivalent of damaged puzzle pieces that cannot be reliably incorporated into the overall puzzle. Singletons comprised 10% of our sequencing reads. *Id.* While tens of thousands of sequencing reads were unusable, this outcome represented an improvement as compared to other recent 454 transcriptome assemblies where the number of singletons ranged from 13 to 60%. *Id.*

54. We compared the contigs and singletons to known protein sequences. *Id.*, .0005. Because a few thousand singletons returned matches to known proteins, we combined the contig and singleton matches to construct clusters of nucleic acid sequences that allowed us to reconstruct the coral transcriptome. Where assembled sequences matched genes in public databases, we annotated the genes to demonstrate coverage. *Id.*, .0006. From there, we compared the completeness and depth of coverage of our sequencing results to known metabolic pathways, sequences of closely related organisms, and to similar research papers. Through these

comparisons, we confirmed the completeness of our assembled transcriptome and "the potential for our method to improve sequencing depth and efficiency in future transcriptome sequencing efforts." *Id.*, .0010.

B. Evaluating the 3'-end Bias

55. To test how effective our method was in avoiding a bias towards the 3'-ends of transcripts and in preventing their under-representation due to the "poly-A blinding" problem, we examined how many raw reads contained a single copy of the "broken chain" T sequence. Of the 628,649 raw sequencing reads (EX1006.0002), 98,276 raw reads contained a single copy of the "broken chain" T sequence. That is approximately 15.6% of total raw reads (we report 16% in Meyer). *Id.*, .0009.

56. In isolation, that number alone was not useful to us. We were interested in knowing whether our methods improved on the 454 sequencer and reduced known sequencing errors. To see if our methods succeeded, we compared that number to what we expected might have been the outcome based on a few assumptions.

57. First, we assumed that the average read length of the raw reads (232 nucleotides) was reflective of the population. *See id.*, .0009. As we reported in Meyer, the length of the raw reads ranged from 30 to 474 nucleotides with a standard deviation of 55 nucleotides. *Id.*, .0002.

58. Second, we assumed that the average transcript size was 2,200 nucleotides. *Id.*, .0009. I believe this number was based on the average mRNA

length in mammals, which had been reported to be 2,200 nucleotides. EX2080. Thus, on average we expected to have about 10 fragments (2,200/232) per transcript. Since only one of these fragments would contain a poly-A tail, the fraction of reads with the "broken-T" sequence was expected to be about 10%. The value that we observed, 16%, was a good match to this very approximate "ballpark" estimate: we were happy to find that our method was not off by several fold in terms of over- or under-representation of 3'-end fragments. After all, the goal of the method was to avoid ***any*** bias in representation of different parts of transcripts. If we wanted to formally test whether 16% actually constitutes enrichment of the 3'-ends, it would have required a much more sophisticated calculation of the expected fraction of 3'-ends, based on the whole distribution of the lengths of actual coral (rather than mammalian) transcripts as well as the distribution of the length of the reads.

C. SNP Validation

59. After sequencing the transcripts and assembling the transcriptome, we also separately evaluated the number of SNPs that were present in the sequencing data. Using a newly developed software program (QualitySNP), we identified around 30,000 potential SNPs. *Id.*, .0009.

60. To confirm the accuracy of the predicted SNPs, we selectively enriched for and sequenced 20 SNPs. *Id.* We used target-specific primer pairs to target and enrich for each SNP. These primer pairs were reported in Additional File 3 (*see*

id., .0017, which I understand was not included in Exhibit 1006. I also understand that Additional File 3 has now been submitted as Exhibit 2079. I have reviewed that version and can confirm that it is a complete and accurate copy of Additional File 3, which was published contemporaneously with Meyer.

61. After we selectively enriched for the 20 SNPs, we confirmed through Sanger sequencing that 70% of the predicted SNPs were accurate. *Id.*, .0009. These findings demonstrated to us the utility of SNP mining from 454 transcriptome sequences. *Id.*, .0012.

VI. MISUNDERSTANDINGS CONCERNING OUR STUDY

62. I understand that IDT's petition makes representations about our study, but several of their positions are incorrect.

A. We Did Not Use the Modified Method in Additional File 4

63. I have been informed by counsel for Tecan that there is a dispute concerning which method was used to obtain the data reported in Meyer. We used the method described in Figure 1. In Additional File 4, we provided a "step-by-step protocol for the library preparation method" outlined in the main article. As we noted, the protocol in Additional File 4 "include[d] minor modifications that we ha[d] recently developed to reduce the number of manipulations required, improve reproducibility, and to further reduce adaptor concatenation." EX1006.0014. As we

also noted in Additional File 4, the minor modifications were to the process for "preparing coral larval cDNA." *Id.*, .0019.

64. The method illustrated in Additional File 4 was not used in the study to generate the data reported in Meyer. *Id.*, .0002. In fact, we stated in Meyer that the cDNA sample "was prepared from coral larvae as illustrated in Figure 1, and sequenced using the 454 GS-Flx platform." *Id.* Any claim that the data reported in Meyer was obtained by the modified method illustrated in Additional File 4 is incorrect.

B. Our Methods Did Not Allow for the Selective Enrichment of Specific cDNA Sequences

65. I have been informed by counsel for Tecan that this study has been used in these proceedings to suggest that the primers targeting the CAP primer and broken chain T sequences (as disclosed in Figure 1 and in Additional File 4) result in the selective enrichment of the end fragments. I disagree. Our goal was precisely the opposite: to obtain data that would represent all genes and all parts of all transcripts as evenly as possible, without any preferences or biases.

66. The use of CAP primers and the template-switching (SMART) procedure is the principal innovation of the Clontech SMART cDNA amplification kit (EX1034), which is designed to promote the best possible evenness of representation for all transcript parts in a set of amplified products. A standard (non-SMART) protocol would produce an over-representation of 3' ends, which the

SMART protocol counteracts in two ways. First, it ensures that only the RNA molecules that were reverse transcribed in their entirety are amplified, and it does not amplify strands that are missing the 5' end. *See, e.g.*, EX1034.0004-05. Second, it suppresses shorter, incomplete transcripts through the use of a single CAP primer for cDNA amplification. *See id.* As we stated in Meyer, our protocol took "advantage of the [SMART cDNA synthesis] PCR Suppression effect to preferentially amplify longer molecules and thus enrich for full-length transcripts" and was designed "to minimize distortions of the samples based on previously described principles." EX1006.0013.

67. We created the broken chain T-primer solely to resolve the "poly-A blinding" problem during 454 sequencing. *Id.*, .0009, .0019. The breaking of the poly-T chain in no way impacted the relative proportion of 3' end fragments that were amplified during library preparation.

68. In the modified method illustrated in Additional File 4, we proposed targeting the broken chain T sequence instead of the CAP primer sequence as a means of reducing the fragment size, which reduced the risk for error and saved sequencing space.

69. Our library preparation scheme (Figure 1) uses CAP primer sequences as anchors to strategically direct the placement of 454 amplification and sequencing primers (A and B), but it does not enrich for any specific part of a transcript. All

fragments with the desired adaptor combination were amplified. We intended for amplification of all fragments because the purpose of our study was to sequence the entire transcriptome as evenly as possible.

70. Our study was not designed to target specific regions of the mRNA transcripts. In order to accurately sequence the entire length of the transcripts, we specifically did not want to enrich certain targets within those transcripts.

71. We chose the SMART cDNA synthesis kit for our coral transcriptome sequencing project because it was designed to isolate and amplify full-length mRNA from a small sample of total RNA, ensuring that the cDNA sample is mostly composed of full-length transcripts and therefore has 5', middle, and 3' end parts of each transcript equally represented. *See* EX1034.0004.

72. In fact, the only discussion in our paper relying on the selective enrichment of target sequences was a separate process not used in Figure 1 or the illustration in Additional File 4. As I mentioned above, after we sequenced the coral transcriptome, we selectively enriched for specific sequences of interest (the 20 SNPs) to validate the accuracy of the sequencing analysis, using PCR with two target-specific primers. *See* EX1006.0009. The primer pairs were reported in Additional File 3. *See* EX2079. We needed to use a different method to target and enrich for these SNPs because the methods used for preparing our coral

transcriptome library were not designed for target enrichment. We also needed to use separate target-specific primer pairs to enrich for specific sequences.

C. Our Data Does Not Show Target Enrichment

73. I have also been informed by counsel for Tecan that the data reported at EX1006.0009 has been interpreted to demonstrate enrichment of the sequencing library ("A single copy of this 'broken-T' adaptor was found in 98,276 of the raw reads (16% of the total), slightly more than the expectation (~10%)"). That is not an accurate conclusion based on our work or Meyer.

74. As I explained above, the prediction of the expected fraction of 3' end fragments (10%) is an approximation, and 16% is well within the limits of its uncertainty. This was not a measure of enrichment but a way for confirming that the broken chain T sequence appeared within a reasonable amount of sequencing reads. Nor could it have been a measure of enrichment. To ascertain enrichment, a much more sophisticated calculation of the predicted fraction would be necessary, based on the knowledge of the length distribution of actual coral mRNAs that can only be obtained after whole-genome sequencing. In addition, the method we actually used (as described in Figure 1) did not even use the broken chain T sequence as an anchor to attach the 454 adaptors A and B. *See* EX1006.0002-03. Once again, we designed both methods to amplify all fragment types to ensure that our data captured the entire transcriptome, as described above.

75. The approximate match between the observed and expected fraction of 3' end fragments was meant to demonstrate that our method resolved the 454 sequencer's "poly-A blinding" problem, which would have led to the under-representation of 3' ends. We also wanted to ensure that the 3' end was not overly represented (why we used the SMART protocol in the first place, which allowed for us to focus on the homopolymer optical issue instead). The data does not reflect the inadvertent enrichment of the 3' end fragment over other cDNA fragments during amplification: as I explained above, the approximate, back-of-the-envelope nature of our prediction of expected sequences (10%) simply cannot support such an inference. We also never reported in Meyer on the number of 5' end fragments or internal fragments for comparison.

76. As we explained in Meyer, we examined the number of sequence reads with the broken chain T sequence because we were concerned that the 3' end fragments would be underrepresented in the data given the 454 sequencer's struggles with homopolymers. *See* EX1006.0009. The 454 sequencer's homopolymer sequencing issue was known to result in high levels of underrepresentation for affected sequencing reads—sometimes to the point that specific sequencing reads appeared almost non-existent in the data. Given this profound potential impact on the data, we felt that results that were in the ballpark range of what we estimated would reflect success.

77. Any suggestion that the data reflects an enrichment of the 3' end fragments over the other cDNA fragments in our library of fragments that were sequenced misinterprets what we actually reported in Meyer.

VII. CONCLUSION

78. I declare under penalty of perjury that the foregoing is true and correct.

Executed on July 17, 2025, at Austin, Texas.

Mikhail V. Matz, Ph.D.

EXHIBIT A

NAME	POSITION TITLE
Mikhail V. Matz	Professor

EDUCATION / TRAINING

INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
Moscow State University, Moscow, USSR	B.S.	1989	Molecular biology
Moscow State University, Moscow, USSR	M.S.	1991	Molecular biology, protein science
Institute of Bioorganic Chemistry, Moscow, Russia	Ph.D.	1999	Biochemistry

Google Scholar Citations: http://scholar.google.com/citations?user=VB83XasAAAAJ&hl=en
Lab web page: http://matzlab.weebly.com/

Summary of Research Interests

I am interested in how organisms adapt to environmental variation throughout their range and through time at the genomic level. My lab focuses on molecular adaptation, gene regulation, and epigenetics of reef-building corals. We also develop novel laboratory and bioinformatic methods for genomic analysis on non-model organisms.

Previously, I have made key contributions to development of genetically encoded fluorescent markers of the Green Fluorescent Protein (GFP) family, beginning with introduction of multi-colored proteins of that kind to biotechnology in 1999 and followed by studies of their diversity and evolution in 2000-2010.

Professional positions

Professor, 08/19 – present, Department of Integrative Biology, the University of Texas at Austin
Associate Professor, 08/12 – 08/19, Department of Integrative Biology, the University of Texas at Austin
Assistant Professor, 08/06 – 08/12, Section of Integrative Biology, the University of Texas at Austin
Research Assistant Professor, 05/01 – 08/06, Whitney Laboratory for Marine Bioscience, University of Florida, St Augustine FL 32080 (joint appointment: Assistant Scientist, Department of Molecular Genetics and Microbiology, University of Florida)
Postdoctoral associate, 10/00 – 05/01, Whitney lab, University of Florida, St Augustine FL 32080
Research scientist 1/00-9/00, Institute of Bioorganic Chemistry RAS, Miklukho-Maklaya 16/10, Moscow, Russia
Research scientist 9/99-12/99, Clontech Laboratories Inc., 1020 E. Meadow Cir., Palo Alto, CA, USA
Junior scientist/Research scientist 9/95-9/99, Institute of Bioorganic Chemistry RAS, Miklukho-Maklaya 16/10, Moscow, Russia
Junior scientist 9/91-9/95, Institute of Microbial Genetics, 1st Dorozhny pr., Moscow, USSR

Significant professional activities

- Served on NSF panels "Evolutionary Ecology" (2011), "Ocean Acidification" (2012), "Biological Oceanography" (2018), and "Integrative Organismal Systems" (2021).
- Member of the Genetics Working Group of the Coral Restoration Consortium since 2018.

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- Peer-reviewing of scientific manuscripts: 42 Publons-registered manuscript reviews in the past 5 years
- Notable invited lectures:

"Epigenetics, schmepigenetics: does gene body methylation play a role in adaptation?": Plenary lecture at EPIMAR, 1st Epigenetics in Marine Biology Congress, October 2020.

"Genetics of heat tolerance in reef-building corals": invited lecture at the Gordon Research Conference on Ecological Genomics, University of New England, Biddeford ME, July 2013.

"Methods for detecting genes under selection": invited lecture at the Pan-Pacific Advanced Study Institute (PACASI), Siliman University, Dumaguete, Philippines; July 2012.

"Quantitative genetics and genomics of adaptive traits in reef-building corals": invited lecture at the Red Sea Research Center symposium, King Abdulla University of Science and Technology (KAUST), April 2011.

"GFP-like proteins illuminate general principles of diversity and complexity evolution": invited lecture at the Nobel Symposium, Copenhagen, Denmark, June 3-7, 2009.

"Ecological genomics": invited lecture at Okazaki Biology Conference, OBC 6 on "Marine Biology", December 2 – 8, 2007.

Awards

Dwight W. and Blanche Faye Reeder Centennial Fellowship in Systematic and Evolutionary Biology, 2009

Major grants

NSF, Biological Oceanography OCE-2433977: The Winning Team: ecological genomics of the great star coral cryptic species complex. PI: Matz, 2024-2027, US $852,591

NSF, Biological Oceanography OCE- 2318775: EAGER: Can ancient DNA illuminate the fate of Caribbean reefs? PI: Matz 2023-2025, US $299,080

Human Frontier Science Program (France): Deconstructing neurobiology of settlement decision-making in coral larvae. PI: Matz, co-PI: Gaspar Jekely (University of Exeter). 2020-2023, US $750,000.

NSF, Integrative Organismal Systems IOS-1755277: Role of gene body methylation in acclimatization and adaptation of a reef-building coral. 2018-2022, $1,117,500

NSF, Biological Oceanography OCE-1801866: COLLABORATIVE RESEARCH: Dynamics of storm-mediated asexual reproduction in Florida Keys corals post-Irma. PI: Kenkel (USC), Co-PI: Matz, 2017-2018, total costs to UT $78,500.

NSF, Biological Oceanography: OCE-1737312: Barriers to cross-shelf coral connectivity in the Florida Keys. PI: Matz, funding period: 2017-2020, total costs $746,000.

NSF, Evolutionary Processes Cluster: DEB-1054766: CAREER: Targets of natural selection in reef-building corals. PI: Matz; funding period: 2011- 2016, $674,000.

NSF, Integrative Organismal Systems: IOS-1052461: Functions of coral fluorescence: an integrative approach. PI: Matz; funding period: 2011-2014, $330,000.

(Co-PI) NIH R01 GM087198: Genetically encoded luminescence. PI: Haddock (MBARI), 2009-2012, UT direct costs $225,000.

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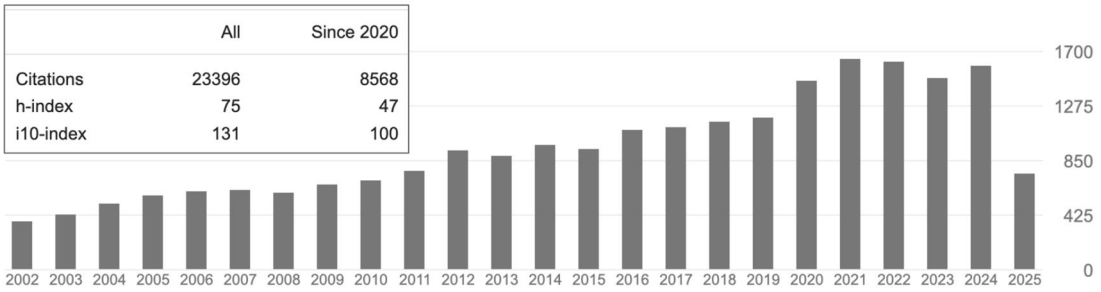
NOAA Coral Reef Conservation Program, NA05OAR4301108: Coral connectivity in Micronesia, PI: Matz, co-PIs: T. Keitt (UT Austin), S. Palumbi (Stanford), 2009-2011, $168,000.

NIH R01 GM078247: Beyond GFP and aequorin: an ocean-wide study of fluorescent and luminous proteins, PI: Matz, co-PI: Haddock (Monterrey Bay Aquarium Research Institute), 2006-2010, $806,000.

(Co-PI) US Department of Defense, PI: Falkowski (Rutgers University),:Analysis of biophysical, optical and genetic diversity of coral reef communities using advanced fluorescence and molecular biology techniques. 2003-2006; direct costs to Matz lab $303,000.

NIH R01 GM066243: GFP-like proteins: diversity and determinants of color, PI: Matz, 2002-2007, $1,115,000

Citation metrics (Google Scholar, as of July 11, 2025)



Non-peer-reviewed publications

Matz, Mikhail. 2024. "'Heroic Interference Should Not Be the Endgame of Coral-Reef Restoration." *Nature* 635 (8039): 551.

Matz, Mikhail V., and Kristina Leilani Black. 2024. "RDAforest: Identifying Environmental Drivers of Polygenic Adaptation." *bioRxiv*. https://doi.org/10.1101/2024.10.21.619525.

Black, Kristina L., John P. Rippe, and Mikhail V. Matz. 2025. "Environmental Drivers of Genetic Adaptation in Two Corals from the Florida Keys." *bioRxiv*. https://doi.org/10.1101/2025.03.03.641296.

Scott, Carly B., Raegen Schott, and Mikhail V. Matz. 2024. "From Juveniles to Giants: Drivers of Holobiont Assembly in Massive Porites." *bioRxiv*. https://doi.org/10.1101/2024.01.09.574877.

Peer-reviewed publications

Legend to categories:

(A) Group leader and principal investigator: Papers in this category were produced under my direct supervision.
(B) Lead author or primary junior researcher: the main person responsible for performing research and preparing the paper, either in as a junior researched supervised by an advisor or as the lead author in a collaboration of peers.
(C) Essential collaborator: made an essential contribution to the project and paper, but did not have primary responsibility for directing or performing the work.
(D) Peripheral collaborator: made a notable, but non-essential contribution to the project and paper.

1. (C) Cabacungan, Gia N., Tharani N. Waduwara Kankanamalage, Amilah F. Azam, Madeleine R. Collins, Abigail R. Arratia, Alexandra N. Gutting, **Mikhail V. Matz**, and Kristina L. Black. 2025. "Cryptic Coral Community Composition across Environmental Gradients." *PloS One* 20 (2): e0318653

2. (A) Black, Kristina L., Line K. Bay, and **Mikhail V. Matz**. 2024. "A Genetic Variant of Delta-9 Desaturase Is Associated with Latitudinal Adaptation in a Coral from the Great Barrier Reef." *Molecular Ecology* 34 (3): e17634.

3. (C) Sanna Y. Eriksson, **Mikhail V. Matz**, Peter D. Vize, Natalie L. Rosser 2024. "Whole genome sequencing reveals genetic differences between Symbiodiniaceae populations among reproductively and geographically isolated Acropora colonies in Western Australia." *Ecology and Evolution*, in press.

4. (B) **Matz, Mikhail V**. 2024. "Not-so-Mutually Beneficial Coral Symbiosis." *Current Biology: CB* 34 (17): R798–801.

5. (A) Scott, Carly B., Annette Ostling, and **Mikhail V. Matz**. 2024. "Should I Stay or Should I Go? Coral Bleaching from the Symbionts' Perspective." *Ecology Letters* 27 (5): e14429.

6. (A) Peterson, Christopher R., Carly B. Scott, Rashin Ghaffari, Groves B. Dixon, and **Mikhail V. Matz**. 2024. "Mixed Patterns of Intergenerational DNA Methylation Inheritance in Acropora." *Molecular Biology and Evolution* https://doi.org/10.1093/molbev/msae008.

7. (A) Abbott, Evelyn, Coral Loockerman, and **Mikhail Matz**. 2024. "Modifications to Gene Body Methylation Do Not Alter Gene Expression Plasticity in a Reef-building Coral." *Evolutionary Applications* 17: e13662.

8. (A) Smith, Samantha K., Galina Aglyamova, Erik W. Oberg, Lee A. Fuiman, and **Mikhail V. Matz**. 2023. "Gene Expression Underlying Variation in the Survival Skills of Red Drum Larvae (Sciaenops Ocellatus)." *Journal of Fish Biology*, June. https://doi.org/10.1111/jfb.15480.

9. (C) Burkhard, Tracy T., **Mikhail Matz**, and Steven M. Phelps. 2023. "Patterns of Repeatability and Heritability in the Songs of Wild Alston's Singing Mice, Scotinomys Teguina." *Animal Behaviour* 200 (June): 91–103.

10. (A) Barfield, Sarah, Sarah W. Davies, and **Mikhail V. Matz**. 2022. "Evidence of Sweepstakes Reproductive Success in a Broadcast-Spawning Coral and Its Implications for Coral Metapopulation Persistence." *Molecular Ecology*, November. https://doi.org/10.1111/mec.16774.

11. (A) Carly B. Scott, Anny Cárdenas, Matthew Mah, Vagheesh M. Narasimhan, Nadin Rohland, Lauren T. Toth, Christian R. Voolstra, David Reich, and **Mikhail V. Matz**. 2022. Millennia-old coral holobiont DNA provides insight into future adaptive trajectories. *Molecular Ecology* https://doi.org/10.1111/mec.16642

12. (A) Dixon, Groves, and **Mikhail Matz**. 2022. "Changes in Gene Body Methylation Do Not Correlate with Changes in Gene Expression in Anthozoa or Hexapoda." *BMC Genomics* 23 (1): 234.

13. (A) Schlecker, Louis, Christopher Page, **Mikhail Matz**, and Rachel M. Wright. 2022. "Mechanisms and Potential Immune Tradeoffs of Accelerated Coral Growth Induced by Microfragmentation." *PeerJ* 10 (March): e13158.

14. (C) Woesik, R. van, T. Shlesinger, A. G. Grottoli, et al. 2022. "Coral-bleaching Responses to Climate Change across Biological Scales." *Global Change Biology*. https://onlinelibrary.wiley.com/doi/abs/10.1111/gcb.16192.

15. (D) Vardi, T., W. C. Hoot, J. Levy, E. Shaver, et al. 2021. "Six Priorities to Advance the Science and Practice of Coral Reef Restoration Worldwide." *Restoration*. https://onlinelibrary.wiley.com/doi/abs/10.1111/rec.13498.

16. (A) Abbott, Evelyn, Groves Dixon, and **Mikhail Matz**. 2021. "Shuffling between *Cladocopium* and *Durusdinium* Extensively Modifies the Physiology of Each Symbiont without Stressing the Coral Host." *Molecular Ecology*, September. https://doi.org/10.1111/mec.16190.

17. (C) Marshall, Thomas L., E. Anne Chambers, **Mikhail V. Matz**, and David M. Hillis. 2021. "How Mito-nuclear Discordance and Geographic Variation Have Confounded Species Boundaries in a Widely Studied Snake." *Molecular Phylogenetics and Evolution* 162 (September): 107194.

18. (A) Rippe, John P., Groves Dixon, Zachary L. Fuller, Yi Liao, and **Mikhail Matz**. 2021. "Environmental Specialization and Cryptic Genetic Divergence in Two Massive Coral Species from the Florida Keys Reef Tract." *Molecular Ecology*, April. https://doi.org/10.1111/mec.15931.

19. (C) Tripp, Joel A., Alejandro Berrio, Lisa A. McGraw, **Mikhail V. Matz**, Jamie K. Davis, Kiyoshi Inoue, James W. Thomas, Larry J. Young, and Steven M. Phelps. 2021. "Comparative Neurotranscriptomics Reveal Widespread Species Differences Associated with Bonding." *BMC Genomics* 22 (1): 399.

20. (A) Dixon, Groves, and **Mikhail Matz**. 2021. "Benchmarking DNA Methylation Assays in a Reef-Building Coral." *Molecular Ecology Resources* 21 (2): 464–77.

21. (A) Kelley, Emma R., Robin S. Sleith, **Mikhail V. Matz**, and Rachel M. Wright. 2020. "Gene Expression Associated with Disease Resistance and Long-Term Growth in a Reef-Building Coral." *Cold Spring Harbor Laboratory*. https://doi.org/10.1101/2020.08.12.248286.

22. (C) Fuller, Zachary L., Veronique J. L. Mocellin, Luke A. Morris, Neal Cantin, Jihanne Shepherd, Luke Sarre, Julie Peng, et al. 2020. "Population Genetics of the Coral *Acropora millepora*: Toward Genomic Prediction of Bleaching." *Science* 369 (6501): eaba4674.

23. (A) Dixon, Groves, Evelyn Abbott, and **Mikhail Matz**. 2020. "Meta-Analysis of the Coral Environmental Stress Response: *Acropora* Corals Show Opposing Responses Depending on Stress Intensity." *Molecular Ecology* 29 (15): 2855–70.

    - ***Perspective***: Bay, Rachael A., and Leslie Guerrero. 2020. "Can Genomes Predict Coral Bleaching?" *Science*.

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24. (B) **Matz, M. V**., E. A. Treml, and B. C. Haller. 2020. "Estimating the Potential for Coral Adaptation to Global Warming across the Indo-West Pacific." *Global Change Biology* 26 (6): 3473–81.

25. (C) Baums, Iliana B., Andrew C. Baker, Sarah W. Davies, Andréa G. Grottoli, Carly D. Kenkel, Sheila A. Kitchen, Ilsa B. Kuffner, et al. 2019. "Considerations for Maximizing the Adaptive Potential of Restored Coral Populations in the Western Atlantic." *Ecological Applications: A Publication of the Ecological Society of America* 29 (8): e01978.

26. (D) A Ali, NG Kriefall, LE Emery, CD Kenkel, **MV Matz**, SW Davies. Recruit symbiosis establishment and Symbiodiniaceae composition influenced by adult corals and reef sediment*. Coral Reefs* 2019, 38: 405-415.

27. (C) Bernal, Moisés A., Groves B. Dixon, **Mikhail V. Matz**, and Luiz A. Rocha. 2019. "Comparative Transcriptomics of Sympatric Species of Coral Reef Fishes (genus: Haemulon)." *PeerJ* 7: e6541.

28. (B) Manzello, D. P., **Matz, M. V**., Enochs, I. C., Valentino, L., Carlton, R. D., Kolodziej, G., Serrano, X., Towle, E. K., Jankulak, M. Role of host genetics and heat tolerant algal symbionts in sustaining populations of the endangered coral *Orbicella faveolata* in the Florida Keys with ocean warming. *Global Change Biology* 2019, 25:1016-1031.

29. (A) Dixon, G. B., Liao, Y., Bay,L. K., and **Matz, M. V.** Role of gene body methylation in acclimatization and adaptation in a basal metazoan. *Proc Natl Acad Sci U S A* 2018, 115: 13342-13346.

30. (A) Quigley, K. M., Strader, M.E., and **Matz, M.V.** Relationship between *Acropora millepora* juvenile fluorescence and composition of newly established *Symbiodinium* assemblage. PeerJ 2018, 6:e5022

31. (A) Barfield, S. J., Aglyamova, G. V., Bay, L. K., and **Matz, M. V.** Contrasting effects of *Symbiodinium* identity on coral host transcriptional profiles across latitudes. *Mol. Ecol.* (2018), doi:10.1111/mec.14774

32. (A) Cleves PA, Strader ME, Bay LK, Pringle JR, **Matz M V**. CRISPR/Cas9-mediated genome editing in a reef-building coral. *Proc Natl Acad Sci U S A* 2018; 201722151.

33. (B) **Matz M V**., Treml EA, Aglyamova G V., Bay LK. Potential and limits for rapid genetic adaptation to warming in a Great Barrier Reef coral. *PLOS Genet* 2018;14: e1007220.

34. (B) **Matz M V**. Fantastic beasts and how to sequence them: Ecological genomics for obscure model organisms. *Trends Genet* 2018;34: 121–132.

35. (D) Berrio A, Guerrero RF, Aglyamova G V., Okhovat M, **Matz M V**., Phelps SM. Complex selection on a regulator of social cognition: Evidence of balancing selection, regulatory interactions and population differentiation in the prairie vole *Avpr1a* locus. *Mol Ecol* 2018;27: 419–431.

36. (A) Strader, M.E, Aglyamova, G.V., **Matz, M.V**. Molecular characterization of larval development from fertilization to metamorphosis in a reef-building coral. *BMC Genomics* 2018, 19:17

37. (D) Rippe JP, **Matz M V**., Green EA, Medina M, Khawaja NZ, Pongwarin T, et al. Population structure and connectivity of the mountainous star coral, *Orbicella faveolata*, throughout the wider Caribbean region. *Ecol Evol* 2017;7: 9234–9246.

38. (C) Torda, G., Donelson, J. M., Aranda, M., Barshis, D. J., Bay, L., Berumen, M. L., et al. Rapid adaptive responses to climate change in corals. *Nature Climate Change* 2017, 7: 627–636.

39. (C) Pollock, F. J., Katz, S. M., van de Water J. A. J. M., Davies, S. W., Hein, M., Torda, G., **Matz, M. V**. et al. Coral larvae for restoration and research: a large-scale method for rearing *Acropora millepora* larvae, inducing settlement, and establishing symbiosis. *PeerJ* 2017;5: e3732.

40. (A) Wright, R. M., Kenkel, C. D., Dunn, C. E., Shilling, E. N., Bay, L. K. and **Matz, M. V.** Intraspecific differences in molecular stress responses and coral pathobiome contribute to mortality under bacterial challenge in *Acropora millepora*. *Scientific Reports* 2017, 7:2610.

41. (A) Davies, S. W., Strader, M. E., Kool, J. T., Kenkel, C. D. and **Matz, M. V.** Modeled differences of coral life-history traits influence the refugium potential of a remote Caribbean reef. *Coral Reefs* 2017, doi:10.1007/s00338-017-1583-8.

42. (D) Oldach, M. J., Workentine, M., **Matz, M. V.**, Fan, T. Y. and Vize, P. D. Transcriptome dynamics over a lunar month in a broadcast spawning acroporid coral. *Molecular Ecology* 2017, 26:2514-2526

43. (A) Kenkel, C. D. and **Matz, M. V.** Gene expression plasticity as a mechanism of coral adaptation to a variable environment. *Nature Ecology & Evolution* 2016, 1: 0014. doi:10.1038/s41559-016-0014

44. (C) Advani, N.K., Kenkel, C.D., Davies, S.W., Parmesan, C., Singer, M.C. and **Matz, M.V.** Variation in heat shock protein expression at the latitudinal range limits of a widely-distributed species, the Glanville fritillary butterfly (*Melitaea cinxia*). *Physiol. Entomol.* 2016, 41:241–248.

45. (A) Dixon, G., Bay, L. K., **Matz, M. V**. Evolutionary consequences of DNA methylation in a basal metazoan. *Mol. Biol. Evol.* 2016, 33: 2285-2293. doi:10.1093/molbev/msw100.

46. (A) Strader ME, Aglyamova G V, **Matz M V.** Red fluorescence in coral larvae is associated with a diapause-like state. *Mol. Ecol.* 2016, 25:559–569.

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