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Dear Editor:

Please consider the manuscript entitled “**Genomic underpinnings of chemosymbiosis in the deep-sea seep-dwelling tubeworm *Lamellibrachia luymesi* (Siboglinidae, Annelida)**” for publication in the journal of ***PNAS***.

Here, we present and characterize the genome of the cold-seep dwelling tubeworm *Lamellibrachia luymesi*, one of the longest-lived invertebrates. Prior to this study, only a few siboglinid endosymbiont genomes have been characterized, genomic resources for hosts remain unexplored. The lack of host genomic hinders understanding of genetic mechanisms involved in how these remarkable animals adapted to extreme environments and host-symbiont associations to different deep-sea chemosynthetic environments.

In particular, we discovered that *L. luymesi* lacks many genes essential in amino acid biosynthesis obligating them to products provided by the symbionts. Interestingly, we found a large expansion of hemoglobin B1 genes many of which possess a free cysteine residue which is hypothesized to function in sulfide-binding. Moreover, sulfide-binding mediated by zinc ions is not conserved across tubeworms, suggesting the hemoglobin structure and the sulfide-binding mechanism is potentially more complex than previously thought. Our comparative analyses also suggest the Toll-like receptor pathway may be essential to host immunity and tolerance/sensitivity to symbionts and pathogens. Last, we identified several genes known to play an important role in longevity. These results help elucidate previously unknown links and potential genetic mechanisms related to the evolution of holobionts, adaptations to reducing environments, and likely extend to other chemosynthetic symbiosis (e.g. deep-sea mussels, clams or shallow water chemosynthetic symbioses).

***PNAS*** would be the best journal for this study as it will be of great interest to a wide variety of scientific fields (e.g., evolutionary biology, deep-sea biology and symbiosis). By characterizing the genome of the seep-dwelling tubeworm *Lamellibrachia luymesi*, we provide genetic evidence of how animals adapted to extreme environments and maintain chemosynthetic symbiosis. Host genome adaptations include loss of biosynthesis pathways, expansion of hemoglobin gene families, innate immunity mechanisms related to host-symbiont recognition, and genes related to longevity. Our findings can be extended to other taxa and shed light on the mechanisms that establish and promote symbiosis, especially in chemosynthetic systems.

Several individuals are appropriate to review this manuscript including:

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No conflict of interest exits in submission of this manuscript, and all authors agree to submit this manuscript to ***PNAS***. On behalf of all co-authors, the work described herein is original research that has not been published, or submitted simultaneously for publication, elsewhere, in whole or in part.

Your consideration of the manuscript is most appreciated, and we look forward to receiving any comments from you or reviewers.

Regards,

Yuanning Li

Ken Halanych

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