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Dear Dr. McFall-Nga:

Please consider the manuscript entitled “**Genomic adaptations to chemosymbiosis in the deep-sea seep-dwelling tubeworm *Lamellibrachia luymesi* (Siboglinidae, Annelida)**” for publication in ***The Proceedings of the National Academy of Sciences U.S.A* (*PNAS*)*.***

We discovered that *Lamellibrachia luymesi*, a common chemosynthetic tubeworm that lives at cold-seeps in the Gulf of Mexico, has several genomic adaptations to facilitate symbiosis. To date, genomic studies of adaptation and evolution in obligate endosymbiosis have focused mainly on modifications found in the endosymbiont (e.g., the bacteria in bacterial-animal symbioses). Herein, we show several genomic adaptions that implicate cellular mechanisms in the host organism. Such host genomic adaptions include loss of essential genes used in amino acid biosynthesis obligating tubeworms to use products provided by endosymbionts and a large expansion of hemoglobin B1 genes which aids transport of H2S to endosymbionts. We also explore the Toll-like receptor pathway involved in host immunity and tolerance to symbionts, and several genes known to play an important role in longevity are identified. These findings are based on *L. luymesi’*s complete genome (one of the most complete Lophotrochozoan genomes to date) as well as transcriptomes and proteomic data.

These findings help elucidate the genetic mechanisms related to the evolution of holobionts and adaptations to reducing environments. Importantly, our results also hold implications for other symbiotic systems, specially chemosynthetic symbiosis (e.g. deep-sea mussels, shallow water clams, hydrothermal vent shrimp, etc). Thus, ***PNAS*** is the best journal for this study given the broad interest to a wide variety of scientific fields (e.g., evolutionary biology, deep-sea biology and symbiosis).

Several individuals are appropriate to review this manuscript including:

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| --- | --- | --- |
| Dr. Jillian Petersen | University of Vienna | [petersen@microbial-ecology.net](mailto:petersen@microbial-ecology.net) |
| Dr. Chuck Fisher | The Pennsylvania State University | [cfisher@psu.edu](mailto:cfisher@psu.edu) |
| Dr. Christoph Bleidorn | University of Leipzig | [bleidorn@uni-leipzig.de](mailto:bleidorn@uni-leipzig.de) |

Two individuals are non-preferred to review this manuscript since they are working on similar project as this manuscript.

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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.

Regards,

Yuanning Li

Ken Halanych

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