Vol. 21, e211012 (2024)
doi: 10.2142/biophysico.bppb-v21.s012

Biophysics and Physicobiology
https://www.jstage.jst.go.jp/browse/biophysico/

Special Issue: Singularity Biology and Beyond

Commentary and Perspective (Invited)

Model systems for discovering evolutionary singularity of bilaterian physiological regulation: lessons from studies on simple/primitive flatworms

Shunsuke Mori, Aoshi Kobayashi, Hirotaka Sakamoto, Mayuko Hamada, Tatsuya Sakamoto, Ryo Nakamura

Ushimado Marine Institute (UMI), Okayama University, Setouchi, Okayama 701-4303, Japan

Received December 30, 2023, year; Accepted February 29, 2024;
Released online in J-STAGE as advance publication March 2, 2024
Edited by Hiroko Bannai

Bilaterians emerged approximately 550 million years ago, and have evolved a variety of morphologies, ecologies and physiologies. The shared characteristics governing physiological processes (e.g., body fluid homeostasis and active behavior) across various bilaterians imply the existence of common mechanisms underlying the functional diversity of physiological systems in bilaterians. Specifically, the acquisition of integrated control mechanisms represents a "singularity" that manifested in their common ancestors. To understand this singularity, informative models can be found in simple/primitive flatworms, such as acoels (Xenacoelomorpha) and planarians (Platyhelminthes). These organisms are considered to be positioned at the base of the evolutionary tree of deuterostomes (e.g., vertebrates and invertebrate chordates, hemichordates, and echinoderms) and protostomes (e.g., arthropods, nematodes, mollusks, and annelids), respectively ([1], Figure 1A).

While the characteristics of the common ancestor of bilaterians (“urbilaterian”) are still a matter of debate, the simple morphologies of these flatworms, featuring a blind gut with only one ventral opening and a basic central nervous system without a coelom or a circulatory system, suggest a possible urbilaterian morphology [2,3]. Moreover, the evolutionary origins of neuropeptide/hormone systems, believed to have emerged with the “brain” and serving as pivotal regulators of behaviour/homeostasis, can be traced back to these flatworms [4,5]. Examination of other bilaterian orthologous genes in flatworms also reveals molecular similarities to various bilaterian lineages. For example, cAMP-dependent protein kinase A catalytic subunit (*PKA-C*) / *DC0*, calcium/calmodulin-dependent protein kinase II (*CaMKII*), and 14-3-3ζ/*Leonardo*, all implicated in learning/memory circuits in mammalian hippocampus and/or insect mushroom bodies, as well as those involved in photoreceptors (e.g., *Opsin*) are also expressed in their corresponding architectures ([6], Figure 1B-F). Collectively, these data underscore the significance of studying of flatworms to elucidate the prototype of the bilaterian ancestral node.

Furthermore, it remains largely unexplored whether physiological regulation (i.e., those mediated by neuropeptide signaling molecules) observed in Bilateria also functionally exists in the outgroup of Bilateria. Identifying similar regulation in non-bilaterian phyla could offer novel insights into the evolutionary origins of the bilaterian systems [7]. Integrating studies of these newer and traditional model systems will facilitate a comprehensive understanding of the singularity during evolution. Indeed, flatworms are easy to be maintained in a laboratory, and their simple body system will contribute to the understanding the physiological processes. Finally, recent advances in genomics and application tools for probing their genome, cellular activity, and physiology, in collaboration with the University of Otago (New Zealand, flatworms, [5]), the University of Oxford (UK, flatworms, [5]), Station Biologique de Roscoff (France, acoels), and Academia Sinica (Taiwan, acoels), among others, will enable us to dive deeply into the field of singularity related to the evolutionary studies in the future.

Corresponding author: Shunsuke Mori, Ushimado Marine Institute (UMI), Okayama University, 130-17, Kashino, Setouchi, Okayama 701-4303, Japan. ORCID iD: https://orcid.org/0009-0009-5327-3874, e-mail: pas058j0@s.okayama-u.ac.jp

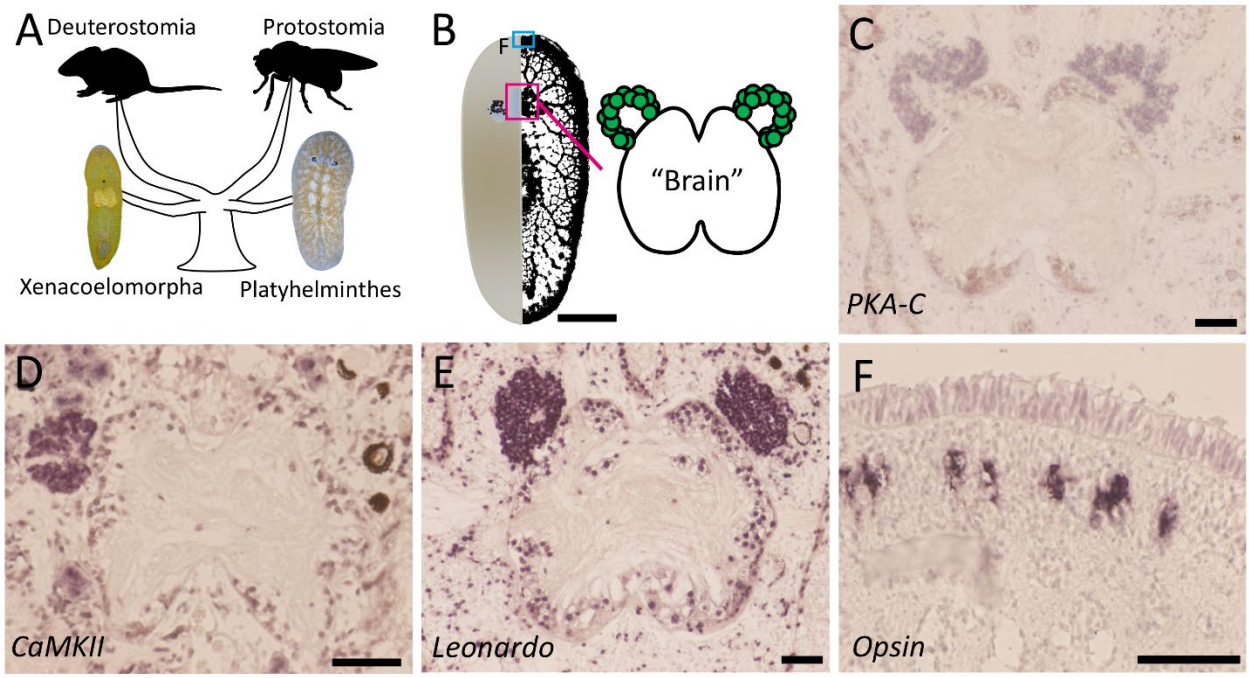

Figure 1 (A) The phylogenetic relationships in Bilateria. Note that Xenacoelomorpha (acoel) and Platyhelminthes (marine planarian) are basal phyla in Deuterostomia and Protostomia, respectively. (B) Neuronal organization in the marine planarians (*Stylochoplana pusilla/Notoplana humilis*) with a "brain". Regions corresponding to the mushroom-body/hippocampus ground pattern are shown in green (Ikenaga, T., Kobayashi, A., Takeuchi, A., Uesugi, K., Maezawa, T., Shibata, N., et al., unpublished data). (C-E) In situ hybridization data of the brains showing the strong expression of *PKA-C* in the "mushroom body" of *N. humilis*. The robust expression patterns of *Leonardo* (*N. humilis*) and *CaMKII* (*S. pusilla*) are similar to that of *PKA-C*. (F) At the anterior end of the *S. pusilla* indicated in (B), *Opsin* is expressed as well as in the eye spots. Scale bars: (B) 500 μm; (C-F) 50 μm.

References

[1] Cannon, J. T., Vellutini, B. C., Smith, J., Ronquist, F., Jondelius, U., Hejnol, A. Xenacoelomorpha is the sister group to Nephrozoa. Nature 530, 89–93 (2016). https://doi.org/10.1038/nature16520

[2] Hejnol, A., Martindale, M. Q. Acoel development supports a simple planula-like urbilaterian. Philos. Trans. R. Soc. Lond. B Biol. Sci. 363, 1493–1501 (2008). https://doi.org/10.1098/rstb.2007.2239

[3] Quiroga, S. Y., Carolina Bonilla, E., Marcela Bolaños, D., Carbayo, F., Litvaitis, M. K., Brown, F. D. Evolution of flatworm central nervous systems: Insights from polyclads. Genet. Mol. Biol. 38, 233–248 (2015). https://doi.org/10.1590/S1415-475738320150013

[4] Thiel, D., Franz-Wachtel, M., Aguilera, F., Hejnol, A. Xenacoelomorph neuropeptidomes reveal a major expansion of neuropeptide systems during early bilaterian evolution. Mol. Biol. Evol. 35, 2528–2543 (2018). https://doi.org/10.1093/molbev/msy160

[5] Kobayashi, A., Hamada, M., Yoshida, M., Kobayashi, Y., Tsutsui, N., Sekiguchi, T., et al. Vasopressin-oxytocin–type signaling is ancient and has a conserved water homeostasis role in euryhaline marine planarians. Sci. Adv. 8, eabk0331 (2022). https://doi.org/10.1126/sciadv.abk0331

[6] Wolff, G. H., Strausfeld, N. J. Genealogical correspondence of a forebrain centre implies an executive brain in the protostome–deuterostome bilaterian ancestor. Philos. Trans. R. Soc. Lond. B Biol. Sci. 371, 20150055 (2016). https://doi.org/10.1098/rstb.2015.0055

[7] Hauser, F., Koch, T. L., Grimmelikhuijzen, C. J. P. Review: The evolution of peptidergic signaling in Cnidaria and Placozoa, including a comparison with Bilateria. Front. Endocrinol. 13, 973862 (2022). https://doi.org/10.3389/fendo.2022.973862