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Preface

Enhancer functions underlying morphological diversity

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Recent progress in the technique of next generation sequencing has been remarkable in uncovering species-specific developmental mechanisms even in non-model animals. In this special issue, we focus on how morphological diversity or species-specific unique morphology was evolutionarily brought about by acquisition of novel enhancer functions, which has been elucidated using analyses of developmental biology and whole genome sequences of various organisms mostly determined by next generation sequencing.

In the past, there was debate about what regions in the genome were responsible for morphological differences among species. Many cases were reported of such genetic causes in coding regions of genes; however, this bias was partly due to the technical difficulty in analyzing noncoding regions. Variations in nucleotide sequences of coding regions and gene copy numbers were well documented because it is easy to establish their association with functions. In contrast, it is very difficult to infer the effects of mutations in gene control regions only from the sequence information, and therefore such effects have been paid less attention or undervalued for a long time. From the early 2000s, the idea that the evolution of *cis*-regulatory sequences in non-coding DNA regions, especially enhancers that upregulate gene expression, contributed to morphological diversification, has become popular (Carroll, 2005; Stern and Orgogozo, 2008). Although alterations of coding regions of developmental genes often disrupt their essential functions, those of enhancers result in addition or deletion of activities with preserving their essential functions. It is also argued that, when considering the structure of the gene regulatory network, evolution of binding sequences of transcription factors on the DNA is much easier than that of DNA binding properties of transcription factors. A growing body of experimental EvoDevo researches has now been showing that various types of morphological diversity are explained by differences in the regulatory regions of genes of interest.

We asked researchers for writing review articles covering a wide range of animals, from invertebrates to vertebrates. The following 10 researchers or groups contributed to this special issue, in which most review articles were based on their latest and remarkable accomplishments.

Kuroiwa (2020) gave an overview of what are emerging themes as a result of recent technological innovations in analyzing the molecular basis of morphological diversity during evolution. Koshikawa (2020) reviewed recent studies on the evolution of

pigmentation patterns in the *Drosophila* wing as an advantageous model for studying the evolutionary mechanism and parallel evolution of traits. Yasuoka (2020) used functional analysis of the *cis*-regulatory module (CRM) of amphioxus as an example to explain how conservation and variability of CRM functions contributed to the evolution of gene regulatory networks in chordates. Liu and Satou (2020) clarified and discussed how the genetic circuit is evolutionarily conserved between ascidians and vertebrates and how genetic programs regulate the regionalization of ectoderm-derived tissues in ascidian embryogenesis. Enny, Flaherty, Mori, Turner and Nakamura (2020) described the evolutionary history of fins of fish, the mechanism of fin development, and the basis of evolution of paired fins, and also described possible developmental constraints on fin evolution. Onimaru (2020) discussed the evolutionary origin of conserved non-coding elements (CNEs) that function as tissue-specific developmental enhancers, particularly focusing on the water-to-land transition during vertebrate evolution. Amano (2020) described how versatile expression patterns of the *Shh* gene are controlled by multiple *cis*-regulatory elements and how vertebrate lineages acquired distinct morphological features. Suzuki and Ochi (2020) summarized their recent study of injury/regeneration-related enhancers, named "regeneration signal-response enhancers (RSREs)," and discussed the mechanism of their activation. Sumiyama and Tanave (2020) introduced the latest findings on the regulation of three *Dlx* "bigene" clusters from the point of view of *cis*-regulatory motifs, TAD (Topologically Associating Domain) boundaries, CTCF loops, and distal enhancer landscapes. Taking the regulatory mechanism of *Hox* gene expression as an example, Saito and Suzuki (2020) discussed how the diversity of skeletal patterns among vertebrate species was brought about.

Thus, in this special issue, we introduce and share the latest findings on how the molecular mechanisms underlying morphological diversity of organisms have been elucidated through the studies of gene regulatory mechanisms. This special issue was based on the symposium "Enhancer function explaining morphological diversity" held on May 17th, 2019, in the 52nd Annual Meeting of the Japanese Society of Developmental Biologists, in Osaka, Japan.

References

- Amano, T. (2020). Gene regulatory landscape of the sonic hedgehog locus in embryonic development. *Development, Growth & Differentiation*, 62, 334-342. <https://doi.org/10.1111/dgd.12668>
- Carroll S. B. (2005). Evolution at two levels: on genes and form. *PLoS Biology*, 3, e245. <https://doi.org/10.1371/journal.pbio.0030245>
- Enny, A., Flaherty, K., Mori, S., Turner, N., & Nakamura, T. (2020). Developmental Constraints on Fin Diversity. *Development, Growth & Differentiation*, 62, 311-325. <https://doi.org/10.1111/dgd.12670>
- Koshikawa, S. (2020). Evolution of wing pigmentation in Drosophila: Diversity, physiological regulation, and cis - regulatory evolution. *Development, Growth & Differentiation*, 62, 269-278. <https://doi.org/10.1111/dgd.12661>
- Kuroiwa, A. (2020). Enhancer, development and evolution. *Development, Growth & Differentiation*, 62, 265-268. <https://doi.org/10.1111/dgd.12683>
- Liu, B. & Satou, Y. (2020) The genetic program to specify ectodermal cells in ascidian embryos. *Development, Growth & Differentiation*, 62, 301-310. <https://doi.org/10.1111/dgd.12660>
- Onimaru, K. (2020). The evolutionary origin of developmental enhancers in vertebrates: Insights from non-model species. *Development, Growth & Differentiation*, 62, 326-333. <https://doi.org/10.1111/dgd.12662>
- Saito, S. & Suzuki, T. (2020). How do signaling and transcription factors regulate both axis elongation and Hox gene expression along the anteroposterior axis? *Development, Growth & Differentiation*, 62, 363-375. <https://doi.org/10.1111/dgd.12682>
- Stern, D. L., & Orgogozo, V. (2008). The loci of evolution: how predictable is genetic evolution? *Evolution*, 62, 2155–2177. <https://doi.org/10.1111/j.1558-5646.2008.00450.x>
- Sumiyama, K. & Tanave, A. (2020). The regulatory landscape of the *Dlx* gene system in branchial arches: Shared characteristics among *Dlx* bigene clusters and evolution. *Development, Growth & Differentiation*, 62, 355-362. <https://doi.org/10.1111/dgd.12671>
- Suzuki N. & Ochi, H. (2020). Regeneration enhancers: A clue to reactivation of developmental genes. *Development, Growth & Differentiation*, 62, 343-354. <https://doi.org/10.1111/dgd.12654>

Yasuoka, Y. (2020). Enhancer evolution in chordates: Lessons from functional analyses of cephalochordate cis-regulatory modules. *Development, Growth & Differentiation*, 62, 279-300. <https://doi.org/10.1111/dgd.12684>