Editorial

A power of comparative genomics

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Armed with its sequence data, comprehensive analyses and bioinformatic tools, comparative genomics have recently become one of the most powerful disciplines in biological sciences. The data gleaned from analyses of genomes in different organisms have had a tremendous impact on almost all disciplines of biological sciences. Of these disciplines, evolutionary and developmental (Evo-Devo) biology has accomplished a recent advancement.[1,2] Evo-Devo is a field of biology that studies developmental processes of different organism to elucidate evolutionary patterns, processes and relationships of different organisms and how developmental processes of different organisms evolved. Evo-Devo of tetrapod limbs, the forelimb (arms) and hindlimb (legs), is one of good examples to illustrate the impact of comparative genomic studies on a recent advancement in Evo-Devo of tetrapod limbs.[1,2]

Including our human limbs, tetrapod limbs have been regarded as a novel structure of tetrapods. Dated back to around three and half million years ago in the Late Devonian, tetrapod limbs had evolved from fish fins.[3,4] Once tetrapod limbs had evolved, the basic structures, the single axis of the skeleton known as the metapterygium with hands and feet, have been conserved throughout different tetrapod groups,[5] yet a number of modifications took place as have been observed in fossil and living tetrapods. Modifications become apparent in the distal parts of limbs, that is, hands and feet with a number of digits.[4] Although humans have five digits in limbs, the number varies among different tetrapod groups. Comparative morphological studies with the fossil data have facilitated developmental and molecular genetic studies on underlying mechanisms for limb development (morphogenesis), particularly in model animals including *Xenopus*, chicken and mice. According to these studies, as embryonic limbs (limb buds) grow, a series of skeletal condensations are formed at a proximal-distal direction and then digit condensations are formed in the distal part of limbs. The patterning of these skeletal elements is controlled by a set of genes including *Hoxd* genes,[1,2,6,7] their specification that sets the stylopod (upper arm or thigh), zeugopod (forearm or calf) and autopod (wrist and fingers or ankle and toes). However, how these genes are regulated for their expressions has remained unclear until comparative genomics has been introduced.

What comparative genomics has contributed to these developmental and molecular studies is particularly a discovery of regulatory elements to control genic expressions and/or interactions among the genes involved in limb morphogenesis.[7] The sequence alignment of homologous genomic regions among different vertebrate groups including tetrapods using VISTA or PIP program has revealed particularly conserved inter-genic regions as Cis-regulatory elements. These regions are now under a close scrutiny for their regulatory roles. For instance, *Hoxd* genes in the mouse *Hoxd* gene cluster have been expressed in the early and late phases during the limb development.[6,7] Now, it is known that the early- and late-phase Cis-regulatory enhancers control these expressions and that the late-phase *Hoxd* gene regulation may have been conserved as a deep homology since the evolution of stem vertebrates.[2] The late-phase *Hoxd* gene regulation was previously regarded unique to tetrapods. Furthermore, the sequence alignment of *Hoxd* gene cluster including the lobe-finned fish coelacanth *Latimeria* has recently discovered that another enhancer region has been conserved only in *Latimeria* and tetrapods examined,[8] suggesting that the fish fin to limb transition might have occurred in the primitive lobe-finned fish groups before landing in the Late Devonian as fossil studies have indicated.

The advancement in comparative genomics has brought our research on evolution and development of tetrapod limbs to a new phase, yet most of the studies have concentrated on underlying skeletal elements as the reference structure for their studies. Since three pairs of six muscles composing mono- and bi-articular muscles in human limbs are known to make a coordinated motion control over the force and direction of limb movements[9] and because these muscles are not present in most of fishes, developmental studies of limb muscles, ligaments and tendons[10] and even nerves[11] will also be critically needed to understand how human limbs evolved among tetrapod groups and how they develop as an unique structure during their embryonic development.

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Conflict of interest

Author declares that there is no conflict of interest.

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