读书报告2

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Title: Limb development: a paradigm of gene regulation.

1st Author: Florence Petit.

This review introduces the mechanisms of gene regulations in limb formation, evolution, regeneration and malformation. ***Formation:***Rostral and caudal Hox signals regulate forelimb and hindlimb specification respectively by regulating *Tbx5* and *Pitx1, Tbx4* expressions*.* TBX4 and TBX5 both support the epithelial–mesenchymal feedback loop involving FGF8 and FGF10. PITX1 is an important transcription factor binding directly to the regulation elements of *Tbx4*. ***Evolution:*** It’s generally accepted that tetrapod’s stylopod and zeugopod have evolved from fish, but the homology of the tetrapod’s autopod and the distal structures of fish fin remains controversial. Many species of tetrapod show altered limb phenotypes, but these changes share two broad similarities: The early limb development is highly conserved among species and certain signaling pathways serve as repeated targets during the evolution of limb development. ***Regeneration:*** Regeneration can be described as a secondary development. Age-related differences in regenerative capacity seem to be related to epigenetic regulation. Methylation and hypomethylation of specific enhancers (such as *Zrs*, the limb-specific enhancer of *Shh*) occur at different developmental stages and thus change the regenerative capacity. ***Malformation:*** Enhancer modulations, gene regulatory rearrangements and chromatin architecture disruptions can cause severe limb malformations. Gene regulatory elements have a major role in the pathogenesis of isolated (non-syndromic) limb malformations and some of the elements can have multiple functions (such as exonic enhancers).

I chose to read this review for three reasons. First, this review provides a comprehensive insight into limb development. It systematically concludes studies on limb development. Besides, the review gives a good example in evo-devo by introducing the genetic relations between limb development and limb evolution. Finally, I have learned many advanced techniques (such as ChIA–PET, RNA-seq, and ChIP–seq) and fundamental concepts in genetics (such as enhancer, promoter, silencer, TAD & accelerated region). The boxes and tips in the review helped me a lot to understand the mechanisms when reading.

In addition to the gene regulation mechanisms above, this review shows the complexity of gene expression and interaction. There are many kinds of cis-regulatory elements in the genome and they interact with genes and each other to activate/repress specific pathways. Genes are blueprints while regulatory elements “determine” how the body is built according to the blueprints. Limb has proven to be an excellent model for organogenesis, gene regulation, and malformation studies. But some topics remain unknown in limb development. For example, the specific sequence changes that cause evolutionary modifications and the pathogenic mechanisms of limb malformations are currently unknown. These unknowns guide the direction of future research.