CDB SEMINAR

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Monday, March 6, 2017

13:30~14:30 A7F Seminar Room

Searching for the molecular basis of human-specific traits and disease

Summary

Human differs from all other vertebrates in many traits. My research program is combining computational screens with vertebrate experimental systems to uncover genes, specific mutations, and mechanisms that cause evolutionary changes in vertebrates. During my seminar, I will first describe a high-resolution genetic mapping experiment we did in threespine sticklebacks, which led to the identification of the gene for a secreted bone morphogenetic protein, Gdf6, as a major locus controlling armor plate size in wild populations. We discovered that freshwater-adapted stickleback populations with reduced size of their armor plates have a *cis*-acting regulatory change that increases *GDF6* expression. Comparative genomics revealed that the human *GDF6* locus also has undergone distinctive *cis*-regulatory evolution, including complete loss of an enhancer that is highly conserved in other mammals. The deletion of this enhancer likely contributed to the evolution of the unique human limb anatomy, including the differential modification of forelimbs and hindlimbs during the transition to bipedalism. These results add to growing evidence that *cis*-regulatory modifications of developmental control genes represent a common mechanism for evolving specific morphological changes in humans and other vertebrates. To take this research further, during the seminar I will outline how we are scanning the human genome for regions that have undergone elevated levels of sequence changes specific to the human lineage with the aim to uncover enhancers, whose human and chimpanzee homologs differ in activity during embryonic development. I will describe how we have already identified a human *RUNX2 cis*-regulatory change that appears to be associated with altered human facial development. I will also show how we are extending this analysis to search the many sequenced mammalian genomes for patterns of repeated genotypic changes and are examining their role in the parallel evolution of particular phenotypes in human and other mammals. Several anatomical transitions that occurred in the human lineage are now the sites of common afflictions in our species, for example, the remarkably high incidence of back and knee problems, the high incidence of complications during childbirth, or the frequent impactation of teeth. Hence, I believe the evolutionary approaches we have taken to identify the molecular basis of human developmental traits will also inform the search for the genetic basis of human disease. I am looking forward to discussing our findings with the research community at RIKEN CDB.

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