Mammalian Evolution: How Mammals Became Mammalian?

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Retroposons such as short interspersed elements (SINEs) and long interspersed elements (LINEs) are the major constituents of higher vertebrate genomes. Altho ugh there are many examples of retroposons acquiring function (exaptation), none have been reported to be involved in the creation of morphological innovations specific to a certain taxonomic group. We previously characterized ~100 copies of a SINE family, AmnSINE1, present as a part of conserved non-coding elements (CNEs) in mammalian genomes, proposing that they have acquired genomic functionality, or were exapted after their retroposition, in a common ancestor of mammals to gain characteristics specific to mammals (1). Here we refined 124 total loci, several of which were analysed further. Using a mouse enhancer assay, we clearly demonstrate that one SINE locus, AS071, 230 kbp from the gene Fgf8 (fibroblast growth factor 8), is an enhancer that recapitula tes Fgf8 expression in two forebrain regions, namely diencephalon and hypothalamus of the developing forebrain. Our gain of function analysis revealed that expression of FGF8 in the diencephalon controls patterning of thalamic nuclei, which are a relay cen ter of the neocortex, suggesting its role in mammalian specific forebrain patterning. Furthermore, we demonstrated that the locus, AS021, 392 kbp from the gene Satb2, controls gene expression in lateral telencephalon, which is suggested as one of the signa ling centers during development (2). Recently, we characterized several more loci which function as enhancers for genes that are expressed in forebrain, suggesting important roles of SINEs in developing the neuronal network highly organized specific to mam mals and introduced by exaptation of AmnSINE1 in a common ancestor of mammals.

Acquisition of some of the phenotypes specific to mammals, such as hair, diaphragm, ear bones, and neocortex, can be dated back before appearance of true placental mammalians a round 120 million years ago (120Ma). P-T extinction event (250 Ma) was very important because early mammals should have been adapted to the atmosphere of low concentration of oxygen after this extinction. Acquisition of diaphragm is one of such adaptation of early mammals. On the other hand, reptiles, represented by dinosaur, also should have been adapted to the atmosphere and dinosaur are believed to have developed the air sac system, a very efficient system of oxygen exchange in lung as we now know it in birds. Due to this efficiency, dinosaur dominated lands in the daytime. Accordingly, early mammals should have to become nocturnal. To live in the night, early mammals should have to develop one mammalian specific phenotype, namely whisker. Whisker is impo rtant to live in the night, because it can function as our hands and can recognize objects without using eyes. This somatosensory system is developed by the help of fgf8, and as shown above the AS071 locus functions as an enhancer of fgf8 to enhance the fo rmation of this somatosensory system in thalamus. Accordingly, we speculate that after P-T mass extinction one of the AmnSINE loci was exapted to be used for enhancer of fgf8 to develop this somatosenmsory system so that early mammals were adapted to the n octurnal life.

(1) Functional non-coding sequences derived from SINEs in the mammalian genome. (2006) Nishihara, Smit and Okada. Genome Res. 16, 864-874

(2) Possible involvement of SINEs in mammalian-specific brain formation. Sasaki et al. (2008) Proc. Nal l. Acad. Sci. USA 105, 4220-4225