Genetic analysis of Jsr (Jumbled spine and ribs) mutation affecting the vertebral development in mice

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The abnormality of the axial skeleton is observed in a various animals including human and mice. Many spontaneous mutants and knockout mice have been contributed to understand these mechanisms of skeletal abnormality. Although the vertebral development was recently reported to be associated with the Notch signaling pathway, these detail mechanisms are uncertain. Jumbled spine and ribs (*Jsr*) mice, which shows the irregular segmentation of axial skeleton, was derived from a spontaneous mutation. As the phenotypes, there are shortening trunk and especially characteristics in the tail. The result of mating experiments shows that this *Jsr* abnormality was due to a single autosomal dominant gene. As a result of high resolution mapping around *Jsr* using 1,026 backcross progeny by mating MOG, *Jsr* was mapped at position 79 cM on the telomere region in chromosome 5 and to the centromeric are a with 0.2 cM apart from marker gene D 5 Mit 292. Furthermore the BAC contig including *Jsr* was constructed in the length of 380 kb (Hasegawa, 1998).

In this study, Lunatic fringe (*Lfng*) and *Uncx 4.1*, which were related genes for the formation of the axial skeleton and located near *Jsr* according to genetic mapping, were suggested to be identified as the candidate gene. Therefore, the sequence analysis of these genes was carried out with using *Jsr* homozygotes. Any mutation causing the amino acid substitution was not found on both *Lfng* and *Uncx 4.1* cDNA, although the locus of *Lfng* was completely corresponded to that of *Jsr* and phenotype of this knockout mouse was very similar to *Jsr*. From these results, *Lfng* and *Uncx 4.1* genes were cancelled to be the causal gene of *Jsr*.

Then, in order to find out the causal gene of *Jsr*, the strategy with the BAC contig including *Jsr* was adopted. The overlapping and each direction of the BAC clone in the contig were examined, and the both ends of the each BAC clone was determined. Although it was indicated that there was some deleted nucleotides in BAC 489-P-1, *Jsr* gene was considered to exist in Sp6 side of the BAC 382-O-7 as a result of the mapping. The causal gene of *Jsr* was expected to be clarified by detailed analysis of BAC 382-O-7 clone in future study.