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Positional cloning in mice: a new mutant mouse, *Sims* (Sexual Immaturity, Megaencephaly, and Seizure)

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Characterization of mutant mice has been utilized as an animal model for the study of human inherited diseases. In addition to the pathogenesis stduy using the mutant mice, the mice have been used for the identification of the genes causing the phenotypes. Functional cloning and positional cloning are two approaches, depending on the phenotypes of the mutant mice. Though it takes a long time positional cloning has been well used to identify the gene of which function can not be presumed from the mouse phenotype. Recently by the advance of the molecular tools and the human genome project close to 10,000 genetic markers are developed to make the procedure faster.

We obtained a new mutant mouse, sims, spontaneously arose and the affected mouse has a mild tremor and seizure was observed. Homozygote in either sex is sterile since uterus growth in female and seminal vesicle in male are not induced for the growth in puberty, implying the abnormal hormonal regulation during puberty. Supporting this, there is no detectable testosterone in the serum of the mutant male and the brain of the mutant is 30% heavier than littermate. To identify the location of the mutated gene, intraspecies cross to CAST/Ei was carried out and the 37 affected mice was analyzed for the linkage. The gene was mapped on chromosome 18, 20 cM from the centromere. More than 500 F2 progenies have been analyzed for the linkage and the locus becomes narrow within 3cM between Egr1 and Fgf gene.