Whole-Genome SNP linkage analysis in a familial multinodular goiter

Introduction: Multinodular goiter (MNG) is a common thyroid disease characterized by diffuse or nodular enlargement of the thyroid gland. Iodine deficiency and smoking have been identified as important environmental factors. However, some studies suggest a strong genetic predisposition. We report the genome-wide linkage analysis using single polymorphism nucleotide (SNP) for a Japanese five-generation MNG pedigree from nonendemic area.

Material and method: The proband was a 15-year-old girl. The ultrasonographic examination showed multiple cystic lesions in the both thyroid lobes and the thyroid hormone was within normal level. The total of 13 blood samples, 7 affected, was obtained from her pedigree. In the five-generation, only one male individual was affected, which was not included in the analysis due to absence of DNA sample. The onset age was 8 to 50 years old. The Illumina HumanCNV370K-Quad Array was used for the whole-genome SNP genotyping. Under assuming fully penetrant dominant mode of inheritance, parametric multipoint linkage analysis was performed using GeneHunter program.

Result: The highest parametric LOD (logarithm of odds) scores were obtained for chromosomes 10q and Xp with values of 2.41 at rs11599135 and 1.80 at rs5933698, and the length of candidate loci were 0.9 Mb and 4.0 Mb, respectively.

Discussion: Previous reports have identified the candidate loci on chromosome 14q (MNG1), Xp22 (MNG2), and 3q26.1-q26.3 (MNG3). In our study, high LOD score was observed on chromosome Xp22, closed to the reported area, but not overlapped. We could not decide a X-linked dominant pattern or not, because the only affected male have no male offspring. However, 10q and Xp22 were new candidate loci for familial multinodular goiter.