

論文の内容の要旨

論文題目

A Genome-Wide Association Study of Knee Osteoarthritis in a Japanese Population

(ゲノムワイド関連解析による日本人集団における変形性膝関節症疾患感受性遺伝子の探究)

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Knee osteoarthritis, characterized by the degradation of articular cartilage, is the most common form of arthritis in elderly and affecting millions of people worldwide. Although knee osteoarthritis has a strong genetic component, the entire genetic basis for the risk of knee osteoarthritis still remains unclear. A genome-wide association study was conducted in 140 unrelated cases with severe radiographic knee osteoarthritis selected from population based prospective cohorts, and 200 unrelated healthy controls from general population residing in Tokyo, Japan. The most promising variants were evaluated in an independent replication sample sets of 500 cases with severe radiographic knee osteoarthritis and 1489 controls recruited from three distinct cohorts located in three different areas in Japan. All the cases and controls evaluated in this study were of Japanese ancestry. A variant at 3' untranslated region of a gene located at 19q13 was identified with genome-wide significance level (combined p-value = 1.94×10^{-8} , odds ratio (OR) = 1.76 with 95% confidence interval (CI) = 1.45-2.15) that was associated with knee osteoarthritis in the Japanese population. Furthermore, in an analysis of whole mRNA expression data

from gene expression variation database in HapMap individuals, this variant was significantly associated both in Japanese HapMap individuals (p value = 0.006) and in all HapMap populations (p value = 0.043). Moreover, this variant has *cis* effect in an analysis of expression quantitative trait locus effect (q-value = 1×10^{-20}) in public database. Taken together, a novel genetic variant associated with knee osteoarthritis was identified with genome-wide significance level. This result provides the new biological insights in the genetic association for knee osteoarthritis.