Smad3 Gene Polymorphisms and Expression in Serum and Cartilage Influence the Risk of Knee Osteoarthritis

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Purpose: Knee osteoarthritis (OA) is the most common degenerative arthritis that is caused by breakdown of articular cartilage with eventual loss of the cartilage of the joints. Previous study suggested Smad3 gene mutation is a possible predisposing factor for human OA and found gene mutation in OA. In this case control study, we investigated the possible correlation between the single nucleotide polymorphisms (SNPs) SmaI (rs6494629) and FokI (rs2289263) in Smad3 gene, and susceptibility to knee OA.

Methods: Venous blood samples were obtained from all cases as well as controls for genetic analysis. Polymerase chain reaction was performed for SNP analysis using specific primer. Total protein was measured in serum by an enzyme-linked immunosorbent assay (ELISA) method and in cartilage tissue done by Western blot.

Results: A total of 200 cases that confirmed radiographic knee OA and equal number of age and sex-matched healthy controls were enrolled. An SNP (rs6494629 and rs2289263) mapping to intron 1 of Smad3 was associated with knee OA ($P<0.013$ and $P<0.044$, respectively). Serum levels of Smad3 in knee OA patients with rs6494629 TT, CT, and CC genotypes were significantly higher than healthy subjects with the same rs6494629C/T genotypes ($P<0.0001$, $P<0.0006$, $P<0.017$, respectively). Increased serum levels of Smad3 were also observed in knee OA patients with rs2289263 AA, CA, and CC genotypes compared to controls ($P<0.006$, $P<0.0006$, $P<0.004$). We performed Immunoblot analysis on cartilage tissue from 15 cases and 10 controls ($P<0.006$).

Conclusion: Our data indicate that genetic variation in the Smad3 gene is involved in the risk of knee OA. Further we also validated these genetic variations at protein level in both blood and tissue and found significant association.