SUPPLEMENTARY NOTE

Description of the study population and the diagnostic criteria for osteoarthritis (OA)

The Japanese hip and knee OA and control populations were recruited from several medical institutions in Japan, as described previously[1-4]. The Han Chinese knee OA and control populations were recruited as described previously[5] from the Center for Diagnosis and Treatment of Joint Disease and the Center of Physical Examination at Drum Tower Hospital, which is affiliated with the Medical School of China's Nanjing University. Hip OA was diagnosed by orthopedic specialists, based on clinical examinations and radiological findings of joint space narrowing (JSN) and/or osteophytes of the hip joint as previously described[1,2]. Patients with acetabular dysplasia were not excluded, because it is a major cause and predisposing factor of idiopathic hip OA in Japan[6]. Knee OA was diagnosed by orthopedic specialists on the basis of clinical and radiographic findings. For the Japanese knee OA population, we assessed JSN and osteophytes in each subject's knees and graded patients using the JSN scale, which is a modification of the Kellgren and Lawrence grade (KL grade) system[7], as described previously[3,4]. The study included only patients who had a JSN grade of two or higher.

For the Chinese knee OA population, each subject was assessed using the KL grade, and only patients with KL grade of two or higher were included in the study[5]. For both hip and knee OA, rheumatoid arthritis and polyarthritis associated with autoimmune diseases were excluded, as were posttraumatic OA and infection-induced OA. Patients who had clinical and radiographic findings suggestive of skeletal dysplasias (osteochondrodysplasias), including overt short stature, multiple symmetric involvements of epiphyses and a definitely positive Mendelian family history also were excluded from the study[1-5].

For the case-control association analysis of hip OA, we recruited 239 cases and 256 controls for the first screen, and 761 cases and 728 controls for the replication study. The mean ages of the subjects in the first screen were 51.4 for hip OA (range, 20–83) and 62.6 for controls (range, 34–86). Mean ages in the replication study were 55.7 for hip OA (range, 21–84) and 56.2 for controls (range, 20–88). For analysis of knee OA, we recruited 718 cases and 861 controls for the Japanese study, and 313 cases and 485 controls for the Chinese study. Mean ages (years) were: Japanese knee OA, 71.9 (range, 43-93); Japanese control, 49.4 (range, 20-92); Chinese knee OA, 58.8 (range, 21-93); Chinese control, 56.8 (range, 25-97). Additional clinical parameters for each population, including male-female ratio, age and body mass index are detailed in **Supplementary Table 7** online.

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