Report of Deliverable No: D3.1

Grant agreement number 200800

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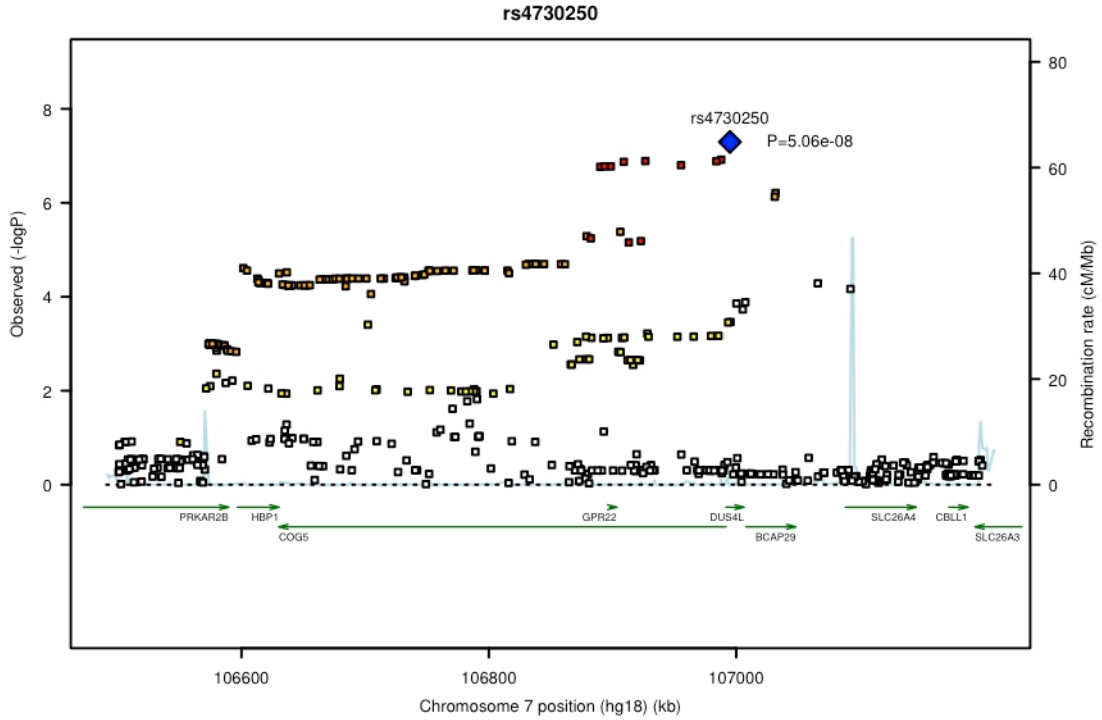
SEVENTH FRAMEWORK PROGRAMME

SEVENTH FRAMEWORK PROGRAMMETHEME HEALTH
FP7-HEALTH-2007-2.4.5-1 Osteoarthritis

Deliverable 3.1 WP3- Meta-analysis of GWA datasets

The meta-analysis of four GWAs from Iceland (deCODE), the Netherlands (Rotterdam study), the UK (Twins UK) and USA (Framingham), was carried out for knee, hip and hand osteoarthritis. By analyzing 2,371 knee OA cases and 35,909 we identified one genome-wide significant locus on chromosome 7q22 for knee OA. The associated signal is located within a large linkage disequilibrium block that contains six genes; PRKAR2B, HPB1, COG5, GPR22, DUS4L and BCAP29 (Figure 1)

Figure 1. Regional association plot of rs4730250.



As a result of the derivable a paper has been submitted and is under review in Annals of rheumatic diseases

‘Evangelou E, Valdes AM, Kerkhof HJ et al. Meta-analysis of genome-wide association studies confirms a susceptibility locus for knee osteoarthritis on chromosome 7q22

Abstract

Osteoarthritis (OA) is the most prevalent form of arthritis and accounts for substantial morbidity and disability, particularly in the elderly. It is characterized by changes in joint structure including degeneration of the articular cartilage and its etiology is multifactorial with a strong postulated genetic component. We performed a meta-analysis of four genome-wide association (GWA) studies of 2,371 knee OA cases and 35,909 controls in Caucasian populations. Replication of the top hits was attempted with data from additional ten replication datasets. With a cumulative sample size of 6,709 cases and 44,439 controls, we identified one genome-wide significant locus on chromosome 7q22 for knee OA (rs4730250, p-value=9.2×10^{-9}), thereby confirming its role as a susceptibility locus for OA. The associated signal is located within a large (500kb) linkage disequilibrium (LD) block that contains six genes; *PRKAR2B* (protein kinase, cAMP-dependent, regulatory, type II, beta), *HPB1* (HMG-box transcription factor 1), *COG5* (component of oligomeric golgi complex 5*), GPR22 (*G protein-coupled receptor 22), *DUS4L* (dihydrouridine synthase 4-like), and *BCAP29 (*the B-cell receptor-associated protein 29). Gene expression analyses of the (six) genes in primary cells derived from different joint tissues confirmed expression of all the genes in the joint environment. *BCAP29, COG5, DUS4L* and *HBP1* expression levels were higher in chondrocyte pellet than in monolayer cultures suggesting that they are expressed in an environment that more accurately recapitulates articular cartilage.