Candidate gene analysis of osteochondrosis in Spanish Purebred horses

Equine osteochondrosis (OC) is a frequent developmental orthopaedic disease (DOD) with high economic impact on the equine industry. The multifactorial origin behind its aetiology, including genetic, vascular or biomechanical influences, as well as other environmental factors such as diet or increased growth, is not completely understood. All these variables complicate the management of this disease that may lead to premature retirement of the animal as a result of chronic pain and lameness. The genetic background of OC includes different genes affecting several locations; however, these genetic associations have been only tested in one or few populations, lacking validation in others.

The Spanish Purebred horse or Andalusian horse, the most ancient horse in the Iberian Peninsula, was involved in the formation of breeds such as Lippizan, Lusitano and native horse American strains and has been bred mainly for classical dressage. Using a candidate gene approach, we have identified the genetic determinants of OC in the Spanish Purebred horse breed by studying the association between loci previously implicated in the onset and development of OC in other breeds and species and different OC locations using radiographic data from 144 individuals belonging to this breed. Among the 48 polymorphisms analysed, three SNP in the FAF1, FCN3 and COL1A2 genes were found significantly or suggestively associated with different locations of OC lesions. The GG genotype of the SNP located in the FAF1 gene was significantly associated with an increase in the prevalence of OC in the right metatarsophalangeal fetlock of 42.7%, when compared with the CC genotype. The gene Fas (TNFRSF6) associated factor 1 (FAF1) has been previously associated with OC lesions score of all joints inspected in pigs. This gene is implicated in apoptosis, negative modulation of osteoblast differentiation and formation and homeostasis of cartilage and bone. The TT genotype of the FCN3 SNP accounts for an increase in the prevalence of OC in the right stifle of 20.1%, when compared with the CC genotype. The gene ficolin (collagen/fibrinogen domain containing) 3 (FCN3), also known as H-ficolin or Hakata antigen, has been previously associated with the presence of OC lesions in fetlock in Hanoverian warmblood horses. FCN3 seems to be an important component of innate immunity, showing a protective activity against bacterial pathogens. Although the involvement of immune response in OC pathogenesis remains unclear, it has been reported that the progression of OC lesions can lead to osteoarthritis, and different functional categories and canonical pathways related to immune responses have been recently implicated in the pathogenesis of OC.

Finally, the genotype TT of the COL1A2 SNP causes an increase in the sum of OC lesions in different locations in the same animal of 30.2%, when compared with the CC genotype. COL1A2 is a component of type I collagen, which is found in most connective tissues, including cartilage, bone and tendon. The increase in the expression of type I collagen (COL1A) in horses has been attributed both to a healing response after the development of OC and to a primary alteration in early lesions reflecting an altered state on the differentiation of chondrocytes. Apart from FCN3

gene that is included in a previously identified quantitative trait locus (QTL), both FAF1 and COL1A2 genes are not included in any reported OC QTL. Given their biological functions, these loci seem suitable functional candidate genes for OC in this breed. These data contribute insights into the complex gene-networks underlying the multifactorial disease OC and the associated SNPs could be used in a marker-assisted selection strategy to improve horse health, welfare and competitive life span.

Natalia Sevane, Susana Dunner, Javier Cañon
Departamento de Producción Animal, Facultad de Veterinaria, Universidad Complutense, Madrid, Spain

Publication

Candidate gene analysis of osteochondrosis in Spanish Purebred horses.
Sevane N, Dunner S, Boado A, Cañon J
Anim Genet. 2016 Oct