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Institute of Genetics and Animal Breeding, Jastrzębiec, Poland

Genetic background of osteochondrosis in the horse – a review*

Dorota Lewczuk, Agnieszka Korwin-Kossakowska**

Institute of Genetics and Animal Breeding Polish Academy of Sciences, Jastrzębiec, 05- 552 Magdalenka, Poland

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Osteochondrosis is considered to be one of the most important problems in European sport horse breeding, as the frequency of OC(D) reaches 25% or more of investigated populations. The present article provides an overview of the genetic background of OC(D) evaluated in different countries. Heritability is low (0.1-0.3) and contemporary selection methods seem not to be sufficiently effective. New approaches regarding molecular methods have been developed and are a promising tool. These include techniques such as whole genome scan, candidate gene analysis and SNP microarrays. Potential candidate genes were found on chromosomes 2, 4, 16, 18, 28 and 30. The most recent results on microarray SNP analysis using 50 000 SNP chip detected new QTL regions in the horse genome.

KEY WORS: genetics / heritability / horse / osteochondrosis / QTL / SNP

Characterization of OC(D)

Osteochondrosis (OC) is a common and clinically important joint disorder described in many domestic species (pigs, dogs, cattle, cats, rats and horses). In fact it is a complex disease regarded as multifactor in origin, comprised by the overall concept of developmental orthopaedic diseases known as DOD [McIlwraith 2004].

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**Corresponding author: a.kossakowska@ighz.pl

Although OC(D) is not new (its first definition was mentioned about 1870), the reasons for its appearance are still not known, and its symptoms are not internationally recognized. Dietary factors, growth rate, anatomic characteristics, trauma and exercise are the main environmental factors that may affect the OC development in growing individuals. The most official and popular definition of OC could be the disturbance in the process of endochondral ossification during skeleton growth [Van Grevenhoff 2011]. During the OC process the ossification does not follow a gradual and regular pattern, but holds back at certain sites, resulting in an irregular ossification front with thick cartilage cones at places. Osteochondrosis affects endochondral ossification of the articular-epiphyseal complex. The ensuing irregularities of the ossification front lead to thick cartilage plugs, the deeper parts of which may become necrotic because nutrition by diffusion becomes insufficient. In the final stage osteochondral fragments may detach and become loose or semiloose intraarticular bodies or joint mice [Van Weeren 2006]. Most of authors recognize two types of the disease – osteochondrosis (OC) as a type of bone developmental disorder without free osseous fragments (1), and a final stage of it (2) in which osseous fragments in the joint form the structure called osteochondrosis desecants (OCD) – Van Weeren [2006]. Muscle-skeleton disorders are of great importance in horse breeding [Esteberg *et al*. 1996]. Among them osteochondrosis is an example of a DOD occurring with an extremely high frequency. Scientific results showed that OC(D) was recognised in 25% [Koenen *et al*. 2000] up to 30% [Stock and Distl 2006] of the investigated horse populations. It was also observed that the percentage of OCD-afflicted horses is growing, and that current selection is not effective enough. A German study reported that in research summarizing the results of all Hanoverian auctions during the period 1991-1998, the prevalence of OC(D) reached 20.5% of horses [Stock *et al.* 2006] and during the years 1991-2003 an increase up to 30.5% was observed [Stock and Distl 2006]. The same authors reported that the prevalence of OCD was observed twice as often in one joint as in two joints simultaneously in one horse [Stock and Distl 2005]; in addition some joints were more afflicted than the others (e.g. the fetlock was more often affected than the stifle). These findings did not comply with a Dutch study [Van Grevenhof 2011], where the fetlock was not the most affected joint, and the left and right joints were homologues. Swedish studies [Jönsson *et al*. 2010] reported that if all horses (with or without clinical signs of disease) were taken into account the frequencies changed significantly from 11 up to 19%. That information seems to be of special importance for breeding strategies against osteochondrosis

In spite of the commonness of this disease, not much is known about its early detection. Investigation concerning the biochemical markers of ossification would help to identify the illness sufficiently early [Lepage *et al*. 2001], but no clear results have been achieved so far. Certain associations between soreness of the bone, its structure and body mass were described by Ribot *et al*. [1995]. Different types of equipment are used for bone illness detection, the most popular is still the x-ray technique of the digital version, but some reports based even on computer tomography have been

published [Lepage *et al*. 2001]. Recently, the results obtained with magnetic resonance [Van Weeren 2006] or less invasive ultrasonography are also available.

Heritability

In spite of its long history, many aspects of the OCD remain unexplained. The first clinical remarks of the condition occurred in 1940, but as the general problem it occurred in the early seventies. Nowadays it is known that the breed most prone to OCD is the Thoroughbred, alongside with Standardbred and sport horse breeds. Some breeds seem to be free from osteochondrosis, such as Shetland Ponies. Clinical manifestations of OCD were recently observed in coldbloods [Wittwer *et al.* 2008], which up to now were thought to be OCD free. It is commonly accepted that osteochondrosis is a complex disease caused by many environmental and genetic influences. Its genetic background was estimated on a very huge range of values of heritability coefficient 0.07 [Report KWPN 1994 in Grevenhof Van 2011] up to 0.65 [Stock and Distl 2006]. Such a wide variability of values is rarely cited, as the range of most estimations is narrower (Tab. 1). Most of the data are estimated on sport horse breeds and the difference between estimations is higher for different joints than for

Table 1. Heritabilities of OC(D) in various sport breeds

Population	Joint	Heritability	Author
KWPN (stallions)	femoropatellar	0.09	Der Kinderen 2005
KWPN (stallions)	tarsocrural	0.11	Der Kinderen 2005
KWPN (mares)	tarsocrural	0.01-0.14	KWPN, 1994
KWPN (yearlings)	femoropatellar	0.02-0.07	Van Grevenhof 2011
KWPN (yearlings)	tarsocrural	0.15-0.36	Van Grevenhof 2011
KWPN (yearlings)	metacarpophalangeal	0.06-0.14	Van Grevenhof 2011
Hanoverian	tarsocrural	0.37	Stock *et al*. 2005
Hanoverian	tarsocrural	0.17-0.28	Stock and Distl 2006
Hanoverian	metacarpophalangeal	0.12	Schober *et al*. 2003
Hanoverian	metacarpophalangeal	0.19	Stock *et al*., 2005
Hanoverian	metacarpophalangeal	0.12-0.17	Stock and Distl 2006
Maremanno	femoropatellar	0.09	Pieramati *et al*. 2003

different breeds. Breeds or locations and/or joints are not the only factors responsible for these differences. Dissimilar data sets, collected from horses of various ages and experience, also provide different results. Heritability estimates depend also on the type of statistical model and programmes used. It seems that heritability estimates based upon linear animal model occur higher than those estimated by linear sires model [Stock and Distl 2006], as well as that wider scale gives higher heritability [Van Grevenhof 2011]. The estimates for OC heritability in the hock range from 0.06 to 0.25 when measured on the visible categorical scale and from 0.20 to 0.40 when transformed to the underlying quantitative scale [Jönsson *et al*. 2011]. Although more publications are required for more detailed summaries, the recent studies show that

OCD heritability increases when older horses with higher sport experience are taken into account [Jönsson *et al*. 2010, Stock *et al*. 2006]. The heritability grew up to 0.46 from the highest level of 0.37 when older horses with sport performance instead of young animals were considered. Swedish studies [Jönsson *et al*. 2011] reported that heritability of osteochondrosis for all horses (with or without clinical signs of disease) measured in the fetlock joint reaches the value of above 0.3, which is quite unusual as normally the fetlock OCD heritability was estimated to be less than 0.1-0.2. Just because of low heritability, the fetlock joint is not considered by selection against OCD in some countries leading in sport horse breeding. Some other problems with estimating heritability appear when the scale of evaluation is considered. A Dutch study showed that computations based on a wider scale of evaluation gave better results as the heritability was higher [Van Grevenhof 2011]. This gives rise to an evident opinion that osteochondrosis should not be scaled as a binary trait, as it is commonly done nowadays. Some differences among European countries might be a result of the different scale used. Even if the five-degree Dutch scale [Grevenhof 2011] seems to be comparable with the four-degree German one [Stock *et al.* 2006], the problem is still not solved. The same applies to new countries which are going to be European-comparable. It is important to mention that the upcoming Scandinavian scaling system of OC could be promising [Jönsson *et al.* 2010].

Even if not enough information is published to discuss certain trends, OCD heritability seems to be higher for the tarsocrural joint (0.11-0.28) than for other joints (0-0.17) – [Van Grevenhof 2011], and osteochondrosis classified as OCD seems to be of higher heritability than the one classified as OC. The high range of heritability values could be caused by various factors [Clausen *et al*. 1990, Björnsdóttir *et al*. 2000], sex [Winter *et al*. 1996; Stock and Dist 2006], type of auction [Winter *et al.* 1996; Stock and Distl 2006], usage type [Stock and Distl 2006], region of breeder and exhibitor [Stock and Distl 2006] or body mass [Stock and Distl 2006]. In view of the great importance of OCD for sport horse production, most leading European countries conduct selection against osteochondrosis as early as possible – primarily before young horses performance tests.

Applied breeding strategies against osteochondrosis are almost the same in most European countries. Selection against OC(D) is conducted in the Netherlands, Germany, France, Sweden, and Denmark, although the procedures and scale are not always identical. Stallions are x-rayed before starting their own performance tests and a result of "osteochondrosis free horse" give them permission to attend performance tests. Until now selection has been based on phenotypic results and was obligatory only for stallions, but breeders are encouraged to test breeding mares as well. Because the OC(D) is a common problem in sport horse breeding, the research was conducted to evaluate possible progress resulting from different selection procedures. Koenen *et al*. [2000] simulated different responses to selection strategies (no selection, selection in stallions only, selection in both sexes). Possible reduction of osteochondrosis ranged from 13% up to 25% in frequencies of ill horses. German research evaluated

the possibility of connected selection on performance and osteochondrosis, based on relations between breeding values for health and performance indexes [Stock *et al.* 2006]. They suggested to incorporate the OCD into the general index of the horse on performance testing [Stock and Distl 2005]. Selection for osteochondrosis seems to be extremely difficult as the heritability of this trait is mostly evaluated on a low level, and the disease seems to be significantly correlated on the genetic background with performance. For different forms of orthopaedic developmental diseases and dressage traits the genetic correlations were estimated at the level from 0.06 do 0.41 and the highest value is noted for OCD; for jumping traits genetic correlations reach values from 0.04 to 0.53 and, as before, the highest value is calculated for OCD as well [Winter *et al.*1996]. Selection is not easier if we consider that genetic correlations between different orthopaedic developmental diseases are negative [Stock and Distl 2006]. Therefore**,** selection based on OCD x-rays even conducted for such a long time by KWPN [1987] and a slightly shorter period in Germany seems not to be entirely sufficient.

Genome mapping and QTL analysis

Due to the prevalence and economic impact of osteochondrosis and because of its low heritability, as well as low efficiency of current selection methods, some international organizations have launched molecular research to identify the genetic background responsible for OCD. Some reports have already been issued and it seems to be proved that the genetic background of that disorder is complex and controlled by a large number of genes [Wittwer *et.al.* 2008]. Starting molecular research for breeding programmes was possible due to the progress in the genetics of the horse, which has developed over the past decade. The first step towards identification of the genomic regions harboring genes responsible for equine OC was the whole genome scans. Integrated genetic maps suitable for the mapping of mutations and traits of interest have been made. In particular the development of the radiation hybrid (RH) map [Chowdhary *et al.* 2003], comprehensive genetic linkage maps [Swinburne *et al.* 2000, 2006] and a medium-density horse gene map [Perrocheau *et al*. 2006] have allowed the localization of type I and II markers. Genetic markers used in genome mapping have been classified on the basis of the level of conservation. Type I markers are these coding markers conserved across different species and typically having low polymorphism. By contrast, type II markers, exemplified by microsatellites, are highly polymorphic ones, invaluable for constructing genetic linkage maps. Historically, genetic linkage maps have been composed largely of type II microsatellite markers and about 1525 polymorphic microsatellites have been mapped [Guerin 1999, 2003, Lindgren *et al* 1998, Penedo *et al.* 2005, Shiue *et al.* 1999, Swinburne *et al*. 2000, 2006]. Genome maps can be used to identify genes or chromosomal regions – *Quantitative Trait Loci*, (QTL) regulating the genetic background of various phenotypic traits.

Efficient generation of the map depends upon the use of a unique mapping reference family. Basic linkage analysis is performed by collecting samples from informative families that segregate the trait under study (ideally 3 generations or large half-sibling families). Molecular markers (most often microsatellite markers) that display differences between individuals are genotyped in the families and the segregation of the marker and the disease is tested.

Most QTL mapping studies for OC(D) were performed during the years 2000-2010 at the University of Hannover. The first genome scan for QTL for osteochondrosis in Hanoverian Warmblood Horse was performed by Lohring [2003]. In total, 27 chromosome-wide QTLs for the OC trait were found on 13 equine chromosomes. In the study by Dierks [2006], 19 chromosome-wide significant QTLs for OC and OCD were located on 17 equine chromosomes: 2, 3, 4, 5, 7, 8, 9, 13, 14, 15, 16, 18, 19, 21, 22, 24 and 30.

Recently, a complete genome scan for OC in Hanoverian Warmblood Horse has shown also QTL for this traits/disease on chromosomes 21, 18, 16, 5 [Lampe 2009] and 2, 4 [Komm 2010]. A whole genome scan was also performed to identify QTL for equine OC using the population of South German Coldblood horses. A whole genome scan for OC in 216 coldblood horses using 250 polymorphic microsatellite markers was performed by Wittwer [2006] and Wittwer *et al*. [2007]. In total 17 putative QTLs located on 17 equine chromosomes were found for OC or OCD in fetlock and/or hock joints. The aim of the study by Wittwer and others was to confirm these QTLs using single nucleotide polymorphisms (SNPs) of genes in this genomic region, and then to test these intragenic SNPs for association with fetlock OC (Tab. 2).

Table 2. Molecular markers found to be important for osteochondrosis disease

Population and material	Methods	Results	Author
Hannoverian	Microsatellites (157)	27 QTLs on 13 chromosomes	Löhring 2003
Hannoverian	Microsatelites (218), SNPs (34)	19 QTLon17chromosomes (ECA2p, ECA4q and other)	Dierks 2006
Hannoverian	Microsatelites (154) SNP (15)	ECA5, ECA16, ECA21, ECA18	Lampe 2009
Hannoverian	Microsatelites (78) SNP (35)	ECA2, ECA4	Komm 2010
South German Cold	Microsatelites (250)	17 QTLs on 17 chromosomes	Wittwer 2007
German Warmblood	Illumina Equine 50k Chip GWA-SNPs	4 QTLs on ECA1, ECA2, ECA3; QTL on ECA3	Distl *et al*. 2009, Klostermann *et al*. 2010
German Warmblood	Illumina Equine 50k, GWA-SNPs	38 QTLs on 17 chromosomes	Distl *et al*. 2010
French Trotters	Illumina Equine 50k Chip	chromosome 3	Blanc *et al*. 2010

Candidate genes analysis

Among the numerous genes identified in the horse genome, it is important to select those called candidate genes, which have their protein products physiologically linked to osteochondrosis. The genes in question are located in the chromosome region suspected of being involved in the expression of a trait such as a disease. Their protein product suggests that it could be the gene involved. The candidate gene can also be identified by association with the phenotype and by linkage analysis done to a region of the genome. To select potential candidate genes, different information can be used. Candidate genes are genes which code for hormones, enzymes, metabolic factors and/or their receptors involved in the complex of cartilage differentiation and maturation during enchondral ossification, in growth processes or in vascularization.

The endocrinological procedures of skeletal growth and development are controlled by hormones that are most likely to participate in enchondral ossification, such as insulin, thyroxin, growth hormone, parathyroid hormone and calcitonin. Of the regulating proteins involved in enchondral ossification, the *Transforming growth factor ß (TGF-ß*) plays an important role in growth cartilage metabolism, particularly in the control of chondrocyte differentiation and hypertrophy [Glade 1986, Henson *et al.* 1997, Jeffcott and Henson 1998]. Henson *et al.* [1997] described a reduced expression and immunoreactivity in focal lesions compared to normal cartilage, but strong expression of *TGF-ß1* in the chondrocyte clusters immediately surrounding a lesion and therefore a possible involvement in the pathogenesis of OC. Semevolos *et al.* [2001] found a higher (but not significant) expression of *TGF-ß* in affected tissue and suggested a healing response to the OC lesion. The *TGF-ß* gene is located on *Equus Caballus Autosome* (ECA)30 and maybe is the potential candidate gene for OC. Another gene – *Insulin-like growth factor* (*IGF)* located on ECA 28, plays an important role in cartilage metabolism and growth, including the introduction of increasing cellular proliferation and the synthesis of cartilage aggrecan and collagen. Foals afflicted with osteochondrosis showed significantly lower IGF-1 levels than those unafflicted. It is suggested that reduced chondrocyte differentiation, caused by lower plasma IGF-1 concentration, may contribute to the development of osteochodrosis [Lampe 2009].

Some of the genes identified in horses were determined using comparative analysis with humans. Good examples are those related to OC located on chromosome 18. A further QTL on ECA18 for hock OC was shown at 78.2-87.6 cM [Wittwer *et al*. 2007]. The region between 45.9 and 87.6 cM on ECA18 is syntenic to human chromosome HSA2q14-q32 [Wagner *et al*. 2006]. This homology between ECA18 and HSA2q had also been shown by other reports [Chowdhary *et al*. 2003; Penedo et al. 2005; Perrocheau *et al*. 2006; Swinburne et al. 2006]. Candidate genes and their location on equine maps could be verified more easily using comparative human-equine maps. In this syntenic region, five candidate genes are located, which were reported to cause conditions in man similar to equine OC and/or are expressed in equine cartilage. The first proposed is *Frizzled related protein (FRZB)* gene which is involved in osteoarthritis in man, and is also expressed in equine cartilage. Mutations

in *COL3A1* and *COL5A2* are associated with human Ehlers-Danlos syndrome. Another gene – *Activin A receptor type 1* (*ACVR1*) is a dimeric growth and differentiation factor of the transforming growth factor, and is also located in this region. An earlier study in man revealed a common and recurrent mutation in the *ACVR1* (617G>A) gene, which causes inherited and sporadic Fibrodysplasia Ossificans Progressiva (FOP) in the global population. The latter gene – *Xin actin-binding repeat containing 2* (*XIRP2*) also known as C*ardiomyopathy-associated protein 3* (*CMYA3*) is also located on HSA2q24.3 and contains 28 Xin repeats which define a novel, repetitive actin-binding motif. Xin protein is found primarily in the intercalated discs of cardiomyocytes and the myotendinous junctions of skeletal muscle cells, both specialized attachment sites of the myofibrillar ends to the sarcolemma. Mutation and expression analyses of the associated gene *XIRP2* will be helpful to clarify the function of this gene in the etiopathogenesis of the OC syndrome in horses. The results by Wittwer *et al*. [2009] indicate that *XIRP2* is a strong candidate responsible for OC and OCD in fetlock and hock joints of coldblood horses.

The recently improved human-equine comparative map for horse chromosome 4 (ECA4) allows comparisons of locations of genes implicated in osteoarthritis in humans for the identified QTL regions on ECA4. Three SNPs located in intron 8, intron 9, and 3′-untranslated region (UTR) of the *Acyloxyacyl hydrolase* (*AOAH*) gene on ECA4q were found to be significantly associated with OCD in fetlock joints [Wittwer *et al.* 2008]. The AOAH is a two-subunit lipase that selectively hydrolyzes secondary fatty acid chains from the lipid region of bacterial endotoxins. Further functions of this gene have not yet been determined. Therefore, the role of AOAH in the development of OC or bone morphogenesis is not clear. Other functional candidate genes for OC located on this chromosome are: the *Carboxypeptidase vitellogenic-like* (*CPVL*), *Anillin actin-binding protein* (*ANLN*), *Engulfment and cell motility 1* (*ELMO1*) Wittwer [2006], and *BMP-binding endothelial regulator* (*BMPER*). The latter gene was shown to be involved in BMP2- and BMP4-dependent osteoblast differentiation and BMP-dependent differentiation of the chondrogenic cells [Binnerts *et al*. 2004].

On chromosome 16, near the significantly associated microsatellite *ABGe049* several *Hyaluronoglucosaminidase genes* are located: *HYAL1, HYAL2* and *HYAL3*. These genes encode a lysosomal hyaluronidase (HYAL1) or a protein which is similar to hyaluronidases (HYAL2 and HYAL3). Hyaluronidases intracellularly degrade hyaluronan, one of the major glycosaminoglycans of the extracellular matrix. Hyaluronan is an important integral structural component of articular cartilage and other tissues, and acts as a lubricant in joints. It contributes to tissue hydrodynamics and movement, cell proliferation, migration and differentiation, and participates in a number of cell surface receptor interactions. Besides the association of hyaluronidases with tumor suppression, mutations in the *HYAL1* gene were found to be associated with mucopolysaccharidosis type IX, or hyaluronidase deficiency [Natowicz *et al.* 1996, Triggs-Raine *et al.* 1999]. Due to their function, *HYAL1, HYAL2* and *HYAL3* genes seem to be suitable functional candidate genes for osteochondrosis [Lampe 2009].

Fine mapping of QTL regions is the condition for localizing associated genetic markers and putative candidate genes on chromosome 2. After bordering the QTL for the different traits of OC, two genes were selected within this region. One is a potential functional candidate gene which might be involved in the development of OC. The *Matrilin 1 gene (MATN*1) encodes the cartilage-specific cartilage matrix protein. Human linkage studies demonstrated that the *MATN*1 gene segregated independently of several heritable chondrodysplasias [Loughlin *et al*. 1994], while Meulenbelt *et al.* [1997] found a significant association between the *MATN*1 gene and radiographically evident osteoarthritis. Second gene – *Collagen, type IX, alpha 2 gene* (*COL9A*2) seems to be a suitable candidate gene for multiple hyaluronan, sciatica and intervertebral disc disease in various mammalian species [Fiedler *et al*. 2002, Holden *et al.* 1999, Annunen *et al.* 1999]. Three previously published by Böneker *et al.* [2006] SNPs within this gene were also selected for genotyping.

SNP microarrays

Nowadays, SNPs are the preferred genetic markers for large-scale genetic mapping projects and have successfully been used to identify chromosome regions associated with complex human and animal diseases. The recent sequencing of the equine genome by an international consortium allows us to identify thousands of SNPs across the genome of the horse [Wade *et al*. 2009]. There are technical platforms that allow genotyping of these SNPs in one individual. Since 2008, a commercially available SNP microarray (*Equine SNP50 Genotyping BeadChip*), which includes 54,602 SNP, enables the genome-wide association analyses, quantitative trait loci (QTL) identification and additionally QTL validation. This chip was developed by Illumina in collaboration with the International Equine Genome Mapping Workshop and the Morris Animal Foundation's Equine Genome Consortium. Designed to enable identification of genes and mutations that contribute to traits of interest in all major horse breeds, this Bead Chip offers a powerful platform for improving horse breeding programmes. It also enables the development of new diagnostic and therapeutic approaches to promote equine health and welfare.

Rather than laborious collection of samples from families, SNPs can be assayed in affected and unaffected animals and genome wide- association analysis can be performed to map traits. This opens up the possibility of mapping many more genes responsible for traits and diseases than was feasible before this technology was available. It is much easier to collect from ill and healthy animals than to collect DNA from large families [Bannasch 2008]. Many authors use the equine SNP chip to investigate common single gene defects and multigenic diseases including musculoskeletal, neuromuscular, cardiovascular and respiratory disorders [Swinburne 2009]. As research begins using genome-wide association studies, many more diseases and traits will be understood at the molecular level in the horse, giving both veterinarians and breeders the tools to eliminate inherited diseases [Bannasch 2008].

Using such microarray technologies leads to great improvement towards unraveling genes underlying QTL for equine OC, and consequently development of a marker test for OC might become available. In order to approve detected QTLs of OC in Hanoverian warmblood horses, a whole genome scan with SNPs was performed. Association and variance analyses enabled the validation of known QTL on ECA 2, 4, 16 and furthermore and the detection of new potential QTL on ECA 3, 7, 19, 20, 22, 26 and 29. Consequently, new potential candidate genes located on various chromosomes were revealed [Komm 2010].

With the great development of biotechnologies, equine molecular genetics has come of age. The recent sequencing of the equine genome by an international consortium is a major advance that will impact equine genomics in the near future. With the rapid progress in equine genetics, new applications in early performance evaluation and the detection of disease markers become available. Many new biomolecular tools will change management of horse selection, disease diagnosis and treatment [Barrey 2010].

Conclusions

The problem of producing OCD-free horses, which some sport horse breeding associations have included in their breeding programmes, seems to be complicated. First of all, it is difficult to conduct international selection for a trait that is not clearly defined. The situation when the stallion free from osteochondrosis in one country could be recognized as OCD-afflicted in the other, is more than difficult for contemporary international horse breeding. Even if the differences between scales used seem to be not very wide, different scales are still a problem to be solved. Some improvement could be done on the level of statistical analysis of population data. Comparison of heritability estimations is also not easy if we take into account that some data are transformed before calculations and others are not, as well as that different statistical analyses are employed in the calculations. This might affect the results significantly. DNA analysis may also have certain limitations as a huge number of genes seems to be involved in the genetic background of osteochondrosis. In any case there is a serious need to breed healthy horses that would undoubtedly benefit from being OCD free, so all possible methods ought to be applied. Heritability values range from 0.1 to 0.3 as well as new potential candidate genes located on identified chromosomes give the possibility of breeding healthy horses.

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