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Review Article

**ANALYTICAL REVIEW OF THE CURRENT STATE THE
GENETIC STUDIES OF BOVINE LEUKEMIA VIRUS (BLV)**¹Larisa Karpenko, ²Petr Ukolov, ³Julia Mukiy, ⁴Olga Sharaskina, ⁵Alesya Bakhta¹St. Petersburg State Academy of Veterinary Medicine, Saint-Petersburg, Russia.**Article Received:** December 2018**Accepted:** February 2019**Published:** March 2019**Abstract:**

International trade in breeding and productive livestock has led to the spread of the BLV leukosis virus in all continents. BLV eradication programs and control measures have been developed in European Union member countries since the second half of the twentieth century, and eradication programs have been very successful in most countries in Western Europe.

The bovine leukemia virus (BLV) causes lymphosarcoma and persistent lymphocytosis (PL). Phylogenetic analysis of the entire genome and the env gp51 strain of BLV showed that BLV can be classified into ten genotypes. Three BLV genotypes, namely genotype-1, genotype-4 and genotype-6, were mainly found throughout the world.

Thus, these results clearly demonstrate that the BLV strain should be determined by complete sequencing of the genome. However, although BLV is present throughout the world, BLV genotyping studies are limited to certain areas, as shown. The accumulation of complete genomic sequencing of BLV strains assigned to different genotypes around the world can determine genotype-dependent pathogenesis and the association between genetic variation in each genotype and its infectivity, and differences in its functions in the future.

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SHORT REVIEW:

International trade in breeding and productive livestock has led to the spread of the BLV leukosis virus in all continents. BLV infection levels vary between and within countries: for example, in dairy herds in the USA: more than 83% of animals are infected with BLV, and the infection level within the herd can be on average almost 50% [1]. In North America, an epidemiological study of the prevalence of BLV in US dairy cattle, conducted by the National Animal Health Monitoring System of the Department of Agriculture, showed that 83.9% of dairy cattle were BLV-positive at the herd level, and 39% of the herds had at least one BLV animal infected. In Canada, studies on the prevalence of BLV showed that up to 37.2% of cows and 89% of herds were BLV-positive [2]. BLV is also present in beef and dairy cattle in Mexico; however, the disease is either absent or limited to specific areas [3]. BLV eradication programs and control measures have been developed in European Union member countries since the second half of the twentieth century, and eradication programs have been very successful in most countries of Western Europe [4]. Indeed, some countries, including Denmark, Finland, Switzerland, Estonia, the Netherlands and Poland, are completely free of BLV [5, 6]. Although most countries in Western Europe are disease free, EBL still exists in Eastern Europe, including Poland, Ukraine and Croatia [7, 8]. In addition, BLV is present in Italy, Portugal, Belarus, Latvia, Greece, Romania and Bulgaria, although the disease is either absent or limited to specific areas. In South America, relatively high levels of BLV were observed, and BLU-induced leukemia is present in most countries. In Brazil, the prevalence of BLV varies in different states, and the infection rate ranges from 17.1% to 60.8%. The prevalence of BLV at the individual and herd levels in Argentina reaches 77.4% and 90.9%, respectively [9]. In addition, infection rates from 19.8% to 54.7% were reported in Chile, Bolivia, Peru, Venezuela, Uruguay, Paraguay, and Colombia [10, 11]. BLV infection is widespread in Chinese dairy farms. Infection rates are up to 49.1% among certain types of dairy cattle, while 1.6% of beef cattle are BLV-positive [12, 13]. Moreover, serological tests showed that 20.1% of yaks in China were BLV-positive. Epidemiological studies in Japan have revealed different levels of BLV prevalence across the country, based on different detection methods [14, 15, 16], as well as the BLV infection rate of 40.9% dairy and 28.7% of cattle, with the incidence rate in animals exceeding 2 years of age reaching 78% in dairy herds and 69% in herds of beef cattle. Less than 6% of cattle were infected with BLV in Mongolia (3.9%), Cambodia (5.3%) and Taiwan (5.8%), while

serological studies in Iran showed a prevalence of BLV of 22 , 1% to 25.4% in this country [17]. Lee and co-authors demonstrated an average prevalence of BLV in Thailand of 58.7%, reaching a maximum of 87.8% and 100% of cattle when analyzed using PCR and ELISA, respectively [17]. In Korea, 54.2% of dairy cattle and 86.8% of dairy herds were BLV-positive, whereas only 0.14% of beef cattle were infected with BLV [17]. BLV infection rates in the Philippines ranged from 4.8% to 9.7% [18], while in Myanmar it was 9.1%. BLV infections in the Middle East are relatively low. The prevalence of BLV infection is approximately 5% in Israel, while in Saudi Arabia 20.2% of dairy cattle are tested for a BLV-positive response. Compared with these countries, the BLV infection rate in Turkey is higher, with 48.3% of dairy herds, including seropositive animals.

The leukemia virus (BLV) causes lymphosarcoma and persistent lymphocytosis (PL). Some polymorphisms of MHC class II genes are associated with resistance and susceptibility to the development of lymphosarcoma and PL, as well as with a reduced number of circulating BLV-infected lymphocytes. Previously, 230 BLV-infected Holstein cows were classified according to two infection profiles, characterized by low and high proviral load (LPL and HPL, respectively). Phylogenetic analysis of the entire genome and the env gp51 strain of BLV showed that BLV can be classified into ten genotypes. Three BLV genotypes, namely genotype-1, genotype-4 and genotype-6, were mainly found worldwide [19]. Genotype-1 is the most dominant genotype of BLV and is distributed in almost all continents, including Europe, America, Asia and Australia. In particular, genotype 1 has spread to South and North America, and these continents still have a high prevalence of infection. In addition, genotype 1 continues to spread throughout the world, including in Asian countries. The second most common genotype is the genotype - 4, which is mainly found in Europe and some American countries. However, it is found only in Mongolia among Asian countries. Interestingly, although genotype-4 existed in Europe, it declined due to the elimination of BLV in European countries. Genotype 6 may have come from South America and spread to South Asia as a result of animal trafficking. Of the other genotypes, genotype 2 is limited to South American countries and is found only in Japan among Asian countries, while genotype 8 is limited to Europe. Genotypes-5 (in Brazil and Costa Rica) and - 10 (in Thailand and Myanmar) are observed only in geographically proximal areas where animals can be exchanged across national borders [17]. In contrast,

genotypes-7 are distributed over geographically dispersed regions [20]. In Europe, five different BLV genotypes were found (genotypes -1, -3, -4, -7, and -8): genotype-4 in Belarus and Belgium; genotypes-4, -7 and -8 in Russia and Ukraine; genotype-8 in Croatia [21]; -4 and -7 genotypes in Poland [21]; genotypes -3 and -4 in France; genotypes -1 and -4 in Germany; and genotype-7 in Italy. In Australia, only genotype-1 was detected. In North America, -1, -3, and -4 genotypes were found in the United States, and genotype-1 was recorded in the Caribbean. In Central America, -1 and -5 genotypes were found in Costa Rica. Different BLV genotypes (-1, -2, -4, -5, -7, and -9) were found in South America: -1, -2, -4, and -6 genotypes in Argentina; -1, -2, -5, -6 and -7 genotypes in Brazil; genotypes -4 and -7 in Chile; genotypes -1, -2, -6 and -9 in Bolivia []; -1, -2 and -6 genotypes in Peru and Paraguay [21]; and genotype-1 in Uruguay. In Asia, a total of seven BLV genotypes (-1, -2, -3, -4, -6, -7, and -10) were confirmed: -1 and -3 genotypes in Korea; genotypes -1, -2 and -3 in Japan; genotypes -1 and -6 in the Philippines; genotypes -1, -6 and -10 in Thailand; genotypes -1, -4, and -7 in Mongolia; genotype-10 in Myanmar; and genotypes -1 and -6 in Jordan [15]. The completion of the sequencing of the entire genome of these BLV strains showed that the BLV genomes contain a number of unique genotype-specific substitutions not only in the env region, but also in the LTR, Gag, Pro, Pol, Tax, Rex, R3, G4, and miRNA-encoding regions, distinguishing each genotype [16]. However, the BLV genome sequences of strains of different geographic origin, especially important regulation sites for BLV virus replication, are relatively stable and highly conservative among BLV strains assigned to different genotypes. On the contrary, several groups recently reported that expression or pathogenesis of BLV does not depend on the strains, but rather is associated with a specific mutation site in their BLV genome [21].

CONCLUSION:

Thus, these results clearly demonstrate that the BLV strain should be determined by complete sequencing of the genome. However, although BLV is present throughout the world, BLV genotyping studies are limited to certain areas, as shown. The accumulation of complete genomic sequencing of BLV strains assigned to different genotypes around the world can determine genotype-dependent pathogenesis and the association between genetic variation in each genotype and its infectivity, and differences in its functions in the future.

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