



Technology Summary: Bovine Leukemia Virus Detection and Prediction

Opportunity Statement

Bovine Leukemia is a viral disease of cattle, also commonly known as BLV, Bovine Leukosis, Lymphosarcoma or Malignant Lymphoma. The virus is associated with the white blood cells called lymphocytes of BLV-infected cows. BLV is transferred from cow-to-cow or cow-to-calf in blood that contains the virus-laden lymphocytes. Very small amounts of blood have been experimentally shown to be capable of transmitting the virus. About 30-40% of US adult cows are blood-test positive for BLV. Out of these, typically 3-5% of infected cows eventually develop tumors of the lymph nodes after a prolonged incubation period.

BLV infections are a major cause of concern among breeders of purebred cattle. Some of the issues faced are:

- a. Significant association between the BLV infection and the occurrence of both clinical and subclinical mastitis;
- b. BLV-infected herds are at a higher risk of hoof problems, gastroenteritis, pneumonia and culling when compared with BLV-free herds;
- c. BLV-positive cows cannot be exported to many foreign countries;
- d. Cost of treatment of BLV cow before a diagnosis is made or suspected;
- e. Loss in milk production;
- f. Increased death loss; and
- g. Condemnation at the slaughterhouse due to the tumors.

According to a study conducted by the National Animal Health Monitoring System (NAHMS,) herds with BLV realize \$59 less in annual production per cow, or 3% less milk, than non-BLV herds. In a Virginia study, the average cost of a case of lymphosarcoma was over \$400. The average annual cost in a 50% prevalence herd was nearly \$6,400 per 100 milking cows.

Commonly used tests for detecting BLV infections, and their corresponding limitations, are:

- **Agar gel immunodiffusion test (AGID)** – The test is not sufficiently sensitive for determining BLV status in many circumstances. The test is also incapable of discriminating infection from adoptive immunity in young calves born from infected cows.

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- **Enzyme-linked immunosorbent assay (ELISA)** -The ELISA test has several shortcomings. Calves up to six or seven months of age may falsely test positive if they have received colostrum/milk with antibodies against BLV. These passive antibodies gradually decay during the first half-year of the calf's life. Additionally, ELISA testing is prone to false negative results, which may occur under various situations including poor antibody response to infection, undetectable antibody levels during early stage of infection and inconclusive test results requiring concentration of the serum.
- **Polymerase Chain Reaction (PCR)** - PCR is not suitable for a herd test. Further, the high sensitivity of the nested PCR may cause problems of false-positive results due to contamination between samples.

One common drawback to all of these alternatives is their inability to identify those cattle that are either resistant or susceptible to the onset of BLV infections. Also, these approaches also can only provide a yes/no answer regarding the presence of the virus and cannot measure increases in the viral levels.

Therefore, there is a need for a solution which addresses the limitations of current approaches and provides a cost-effective, efficient, safe and accurate answer to this growing problem.

360ip's Partner Solution

360ip's partner technology uses a c143 monoclonal antibody for detecting a bovine individual which has a possibility of onset of bovine leukemia. The c143 monoclonal antibody is used for detecting a gene encoding the .beta.1 domain of the bovine MHC Class II DR (beta) chain to which a possibility of onset of bovine leukemia is attributable. A gene encoding bovine MHC Class II DR molecule is amplified by the PCR method, and then reactivity of the monoclonal antibody to the gene product may be investigated. The technique accurately determines the onset of BLV for a large number of bovine individuals.

The technology further relates to exploring the relationship between BLV and the bovine MHC (BoLA) haplotypes, which facilitates, by means of genetic engineering techniques, convenient and accurate judgment of a resistance to the onset of leukemia of a bovine individual caused by BLV. PCR methods are used for the amplification of the DNA genome. Moreover, the technology can accurately and rapidly determine a nucleotide sequence of bovine BoLA-DRB3 exon 2 (BoLA-DRB3.2) and type its genetic polymorphism.

The partner's method for the detection and prediction of the onset of Bovine Leukemia has the following advantages:

1. The method may be applied to a variety of cattle such as dairy cattle, dairy and beef cattle, beef cattle, working cattle, working and beef cattle. A few specific examples of breeds include Holstein, Jersey, Hereford, Aberdeen Angus, Friesian, Japanese Black and Japanese Shorthorn.

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2. The technique conveniently, rapidly and accurately determines the onset of BLV for a large number of bovine individuals. The early detection is vital in curbing the development of enzootic bovine leucosis at a later stage. The detected individuals can be isolated from the rest of the herd, thereby cleansing the herd.
3. Diagnosis of active BLV and predicting resistance/susceptibility to BLV can be achieved all in one sample. Understanding the susceptibility is a key to the future development of a vaccine.
4. The method can be performed using any of the fluorescent antibody methods, flow cytometry, ELISA, immune-histological assay and PCR.
5. The technique can measure increases in viral levels in addition to a yes/no determination.
6. The diagnostic agent containing the monoclonal antibody can be provided in a freeze-dried form or in a liquid form.
7. The diagnostic agent can be prepared by using appropriate additives for formulation (e.g., pH adjusting agents, dissolving aids, antiseptics, buffering agents, excipients, etc.)

Patents

360ip's partner has four families of patents covering multiple jurisdictions.

360ip is seeking interested parties for the licensing, further development and commercialization of this technology-based solution.

For additional information, contact:

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