LA-UR 12-20360

Licensable Technologies

Development of PCR Test-Systems for Highly Pathogenic Avian Influenza Virus Detection on the Territory of the Republic of Kazakhstan

Applications:

- Diagnostic test-systems for avian influenza and swine flu

Benefits:

- Improved surveillance and monitoring of influenza

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Summary:

The work proposed to be completed by LANL and the Kazakhstan Institute for Biological Safety Problems will provide a basis for improving surveillance and monitoring of avian influenza. Kazakhstan's landscape is diverse and HPAI-susceptible bird migration routes pass through the country. Some migrating birds come from areas where AI is endemic. During recent years HPAI has been reported in many regions of Kazakhstan. Availability of up-to-date diagnostic test-systems for AI and swine flu isolate identification and typing is important in their control. Currently, diagnostics use immunoassays and culture to detect and confirm influenza and to perform strain typing. Existing PCR tests make use of available sequence data from characterized strains, however, the utility of many of these assays is limited because the genomic sequence of newly discovered influenza isolates can differ significantly from those previously reported, making some or all of the markers ineffective for detecting the new isolates. Therefore, it is important to collect sequence data from isolates discovered in Kazakhstan to insure that markers and assays are maximally inclusive. It is also important to develop and test new assays for their ability to detect relevant strains, and to distinguish between HPAI, H1N1 strains that infect humans, and other influenza A isolates of interest.

Modern approaches will be used to develop diagnostic test-systems based on PCR to enable detection of influenza A agent in different virus-containing materials, differentiate AI and swine flu viruses from other virus types, and to subtype the agent as H5N1 or H1N1. Multiplex flow cytometry methods will be developed for influenza A virus detection, which will enable diagnosis and prophylaxis. Multiplexed assays provide rapid testing with lower costs and higher confidence in the conclusions drawn from the assays due to higher information content. We will develop assays based on Multiplexed Oligonucleotide Ligation-PCR (U.S. Patent # 7,153,656) for several reasons. One of these is the difficulty of designing real time PCR assays when the genetic diversity among target isolates is high (a characteristic of most RNA viruses, including influenza). Due to the high mutation rates of most RNA viruses, quasispecies clouds of genomic variants occur within an outbreak, with each new virion differing by one or more nucleotides from the original. The high level of variation makes primer and marker design difficult due to limited amounts of highly conserved nucleotide strings. Ligation-based assays are simpler to design using computational tools, and the multiplexed format will allow us to screen many different markers simultaneously at a lower cost per marker. We will attempt to design multiple MOL-PCR markers for detecting and typing influenza A H5N1 and H1N1, and screen them for their utility in a surveillance system.

LANL is currently seeking a commercialization partner to participate in the development of this project.

Development Stage:

LANL and Kazakhstan Institute for Biological Safety Problems are at the initial stages of proposal development.

Patent Status:

No patents have been filed yet for the new work proposed under this project.

Licensing Status:

LANL is currently seeking a commercialization partner to participate in the development of this project. Available for licensing once project is developed.

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