Understanding evolving zoonotic disease threats through genetic sequencing

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In March 2021, the U.S. Department of Agriculture's (USDA) Animal and Plant Health Inspection Service (APHIS) was designated to invest $300 million through the American Rescue Plan Act to conduct monitoring and surveillance of susceptible animals for SARS-CoV-2. Genomic sequencing is the key to better understanding how the genomes of SARS-CoV-2 and other pathogens change in animals over time, which helps the scientific community understand the way that the virus behaves in animals.

"Our goal at APHIS is to work closely with our partners in the diagnostic community to get pathogens sequenced, shared and analyzed in real-time," said Dr. Suelee Robbe-Austerman, APHIS National Veterinary Services Laboratories (NVSL) director. "We are also monitoring the pathogen for key mutations, sharing results with researchers and sending summary data to leaders within animal and public health, which they use to adjust policies and messaging to reflect the most current evidence."

The ability to monitor these ongoing mutations in animal pathogens allows the public health community to analyze and potentially take steps to avoid the risk animal-human transmission of pathogens. While APHIS has been using genetic sequencing tools to detect pathogens in animals and plants for years in support of

disease outbreaks, response and management, APHIS is using the funding from the American Rescue Plan Act to strengthen its national capacity to prevent or limit the next zoonotic disease outbreak or global pandemic.

"The human COVID-19 pandemic and associated animal infections have provided scientists world-wide with new insights into zoonotic threats, reinforcing just how easily viruses can move between humans and the animals we live with and care for," said Dr. John Korslund, APHIS One Health/Office of Interagency Coordination SARS-CoV-2 activities manager. "Now with support from the American Rescue Plan, our agency and its collaborators have a chance to build on knowledge gained with each outbreak to respond more quickly and effectively to new pandemic risks as they appear on the horizon."

Beginning in early 2020, to support APHIS' understanding of the role that animals played in the COVID-19 pandemic, APHIS and its partners quickly utilized existing laboratory capacity at APHIS' NVSL to genetically sequence suspect SARS-CoV-2 samples, consistent with World Organisation for Animal Health (WOAH) guidance. NVSL performs official confirmatory testing and genetic sequencing of animal samples for SARS-CoV-2 and other pathogens. It provides a wide variety of information and services centered around diagnosis of domestic and foreign animal diseases, support of disease control and eradication programs, reagents for diagnostic testing, training and laboratory certification.

NVSL employs a variety of genomic sequencing technologies, ranging from the more basic Sanger methodology to second generation high-through-put short-read platforms, such as Illumina and Ion Torrent, and long-read third generation technologies, such as Nanopore, with selected methodologies appropriate for each application.

"It is extremely rewarding to have such powerful tools at our fingertips," said Robbe-Austerman. "We have seen the results of sequencing alter testing plans, help explain the source of an outbreak, and even reduce and refine the number of animal producers and owners impacted by testing programs."

Veterinarians and researchers send collected SARS-CoV-2 samples to different laboratories depending on the type of animal, clinical signs and current diagnostic programs. While APHIS NVSL serves as the reference laboratory for regulated, high-consequence and reportable diseases, APHIS' partner laboratories also play a critical role in testing animals within the United States and furthering our understanding of

disease patterns and risks of transmission:

- Federal laboratories, such as the APHIS National Wildlife Research Center, U.S. Geological Survey and the Centers for Disease Control and Prevention complete diagnostic testing in some wildlife and other selected cases of concern.
- The National Animal Health Laboratory Network (NAHLN) is a nationwide consortium of laboratories with an APHIS-coordinated and supported role in surveillance, detection, and response testing capacity for foreign animal and reportable diseases, including SARS-CoV-2.
- State and university-supported veterinary laboratories, some of which are part of the NAHLN, regularly test livestock production animal herds for endemic infections and do routine private testing for a wide variety of domestic and zoo animals.
- Privately owned laboratories also support disease diagnostics in the U.S. animal population, particularly companion animals, such as cats and dogs.
- Research laboratories, both domestic and foreign, are used for unknown and emerging pathogen studies, which may provide the first clues to new agents of concern.

NVSL works closely with these laboratory partners to provide U.S. animal owners and producers testing capacity that is complete and coordinated for SARS CoV-2 and other emerging pathogens. Any samples that initially test SARS CoV-2-positive at these partner laboratories may be sent to NVSL for confirmation or further characterization. If official confirmation is not required, laboratories that have the capacity to whole genome sequence can simply share their sequences directly with NVSL to maintain a comprehensive national picture.

"It is just amazing the amount of information shared with this technology," said Robbe-Austerman. "Sequencing files contain a universal language that allow us to communicate across agencies, international trading partners, researchers, and companies. Scientists can take this information and use it to answer uniquely different questions within their mission space."

Funding from the American Rescue Plan Act is providing the support needed for laboratories to contribute to earlier detection of SARS-CoV-2 and reporting of emerging animal and zoonotic diseases. APHIS is also currently conducting multiple projects under the American Rescue Plan Act aimed at understanding how the SARS-CoV-2 virus behaves in different animals, how it moves between animals and people, and what we can do to interrupt transmission.

As the organization expands and enhances its capacities to address the immediate threat of SARS-CoV-2, specialists at APHIS are building critical capacity and enterprise to address future emerging threats and prevent or limit any future pandemics by protecting the health and welfare of the Nation's animals as it has for more than 50 years.

"The COVID-19 pandemic in humans and associated SARS-CoV-2 infections in animals has been an extremely tragic and costly disease episode in U.S. history," said Korslund. "We have the opportunity through hard lessons learned, leveraged by investments such as the American Rescue Plan Act, to build capacities at the molecular level to improve our responses to, or even to prevent the next big zoonotic disease event. We must keep adding to our tools and capacity."

NVSL can sequence any samples meeting basic quality criteria at no cost to the owner or submitting veterinarian. Contact NVSL at NVSL.info@usda.gov for further information.