How a K-State research lab is fighting back against COVID-19

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Kansas State University's Biosecurity Research Institute, a laboratory most known for its high-tech livestock and food-processing research facilities, may seem like an unlikely setting for the fight against COVID-19. Research at the Biosecurity Research Institute typically focuses on pathogens that threaten the food supply by infecting crops or livestock animals.

The novel coronavirus pandemic, and earlier epidemics such as SARS and MERS, has shown that the line between animal and human health is often blurry. Veterinary researchers at the Biosecurity Research Institute have spent their careers planning and preparing to diagnose, prevent, and treat animal disease outbreaks that can threaten the nation's food supply.

Now, they are applying their expertise to the COVID-19 pandemic, making strides in critical areas including vaccine development, drug discovery, and understanding animal susceptibility to the virus.

A 'FORTRESS FOR RESEARCH'

Housed on the K-State campus in Manhattan, the Biosecurity Research Institute has been instrumental in protecting the agricultural supply chain since 2008.

It's one of the most advanced laboratories in the country for studying pathogens that can infect crops, livestock, and food. The research hub contains multiple biosafety level 3 labs — the second-highest possible level of security. The Institute frequently collaborates with government agencies such as the USDA and the Department of Homeland Security to study infectious diseases threatening food security and human health.

"SARS-CoV-2 came along, and we're the only facility that has the safety, the security, the training, the personnel that can do that type of research," said Dr. Stephen Higgs, the director of the Biosecurity Research Institute.

With its complex ventilation system, multiple power backups, and highly trained staff, the Biosecurity Research Institute has been described as a "fortress for research." These engineering features enable its researchers to safely handle dangerous animal and plant pathogens.

The safeguards also allow Biosecurity Research Institute researchers to work with the novel coronavirus itself, a rarity in COVID-19 research.

To prevent researchers from being exposed to the coronavirus, most labs must use "pseudotyped" viruses — viruses unrelated to the coronavirus that are altered to exhibit some of its key features. Being able to work with the real virus makes studies conducted at the Biosecurity Research Institute particularly useful for understanding its behavior and the effectiveness of potential treatments.

NASAL SPRAY VACCINE FOR CORONAVIRUS

Developing a safe and effective vaccine is a critical step in stopping COVID-19's spread.

Dr. Waithaka Mwangi, professor of diagnostic pathobiology in the K-State College of Veterinary Medicine, recently signed an agreement with Tonix Pharmaceuticals to begin preclinical research on a potential COVID-19 vaccine at the Biosecurity Research Institute.

Mwangi's candidate vaccine builds immunity to the novel coronavirus by introducing part of the coronavirus spike protein, the unique component of the virus that binds to human cells. He is using a weakened version of the bovine parainfluenza 3 virus (BPI3V), which doesn't cause sickness in humans, as a vehicle to deliver the spike protein.

Mwangi was not originally intending to create a coronavirus vaccine. Before the pandemic, he was working with the BP3IV technology to create a better vaccine for bovine parainfluenza, a viral illness that commonly affects cattle.

When the COVID-19 pandemic struck, he pivoted. He knew that other versions of BPI3V vaccines had been tested in humans as potential immunizations against illnesses like human parainfluenza, and had been found to be safe. With some adjustments, the BPI3V system might also be able to protect against the novel coronavirus.

What sets Mwangi's BPI3V vaccine apart is that it can be delivered as a nasal spray.

This stimulates an immune response in the cells lining the nose and mouth – the coronavirus's point of entry. The goal is to eradicate the coronavirus before it can spread throughout the body.

Mwangi and his team at the Biosecurity Research Institute have developed a prototype vaccine, and are now conducting preclinical laboratory tests.

SEARCHING FOR A CURE

Veterinary researchers also play a key role in drug development. One of the first steps in determining if a potential medicine will be safe and effective in humans is to test it in animals.

Kansas State University professor Juergen Richt, who has previously led research characterizing the H1N1 swine flu virus, and collaborators at the Sanford Burnham Prebys Medical Discovery Institute in La Jolla, California, are currently conducting preclinical COVID-19 drug research at the Biosecurity Research Institute.

So far, they have identified candidate COVID-19 treatments from a massive library of drug compounds that have already been approved for safe use in humans. After studying the performance of potential medicines in cells grown in the lab, they are now testing the most promising candidates in hamsters.

Hamsters are vulnerable to COVID-19 infection, and are one of the best animal models for understanding the pandemic illness.

The hope is that if one of their drug candidates works well in hamsters, it will be given emergency use authorization approval to move rapidly into human clinical trials.

The antiviral drug remdesivir is currently a main contender for a COVID-19 treatment, but it needs to be administered with an IV drip in a hospital. This requires precious resources and personnel, potentially straining already overloaded hospitals and causing a treatment bottleneck.

Richt and colleagues are focusing on compounds that can be administered orally or as a nasal spray. This would allow patients to take the drug at home, expanding access to treatment and lessening the burden on hospitals.

RULING OUT MOSQUITOES

Containing the coronavirus pandemic also depends on understanding how the disease spreads. Scientists know that the novel coronavirus originated in an animal host, dominantly thought to be a bat, before making the leap to infecting humans. Now, researchers are concerned that humans might transmit the virus to new animal populations.

“Zoonotic diseases go both ways. They go from animals to humans, but humans can bring them back to animals,” explained Richt, who also directs the K-State Center of Excellence for Emerging and Zoonotic Animal Diseases. “This is something that can change the epidemiology of the disease.”

The mathematical models that epidemiologists use to predict the spread of the coronavirus don’t account for transmission of the virus from animals to humans – if animals can transfer the disease to humans, it could fundamentally change predictions of the virus’s spread.

Work at the Biosecurity Research Institute offers some relieving news.

In a study published this month, a group of Biosecurity Research Institute researchers showed that the coronavirus cannot replicate inside of common mosquito species. That means that if a mosquito bites an infected person, it cannot spread COVID-19 to other people it bites.

Richt has found that pigs don’t seem susceptible to the virus either. His future research will focus on the potential for other animals, such as cats, to become infected with and spread COVID-19. Richt is also seeking funding to examine the vulnerability of sheep and cattle.

Mwangi, the vaccine researcher, is hopeful that the collaborative research efforts at the Biosecurity Research Institute, and around the world, will bring about the end of the COVID-19 pandemic.

“I don’t think this is the first time that humanity has dealt with such an issue,” he reflected. “Something positive will come out.”