

SYNTHETIC NANOVACCINES PROTECT AGAINST RESPIRATORY PATHOGENS





To protect soldiers against airborne bacterial pathogens and chemical weapons engineered to attack the central nervous system, UNMC is collaborating with Iowa State University (ISU) to develop single dose vaccines that boost the immune system.

The five-year, \$3.4 million grant from the U.S. Army also has been an exercise in Congressional collaboration as Sen. Ben Nelson worked with Iowa Sens. Chuck Grassley and Tom Harkin to secure continued funding for the project that began in 2008. The funds are equally divided between two institutions.

“This valuable collaboration taps expertise on both campuses,” said Mark Bowen, director of government relations at UNMC. “It has military and civilian applications — it benefits everyone. Chemicals used in agriculture are the same as those used in warfare for biological weapons, just mixed differently.”

The researchers evaluate three novel nanotechnology platforms based on safe and degradable adjuvant polymer systems that enhance antigen presentation and stimulate immunity.

The first target: H5N1, or avian flu, a significant pandemic threat when it quickly spread around the world, reaching a peak in 2006. H5N1 is highly contagious and mutates quickly. Last year, 17 countries throughout Europe, Asia, Africa and the Middle East reported outbreaks of H5N1 in domestic poultry and wild birds.

So far, the spread of H5N1 virus from person-to-person has been rare, limited and unsustainable. The World Health Organization reports that overall mortality in reported H5N1 cases is approximately 60 percent. The majority of cases have

occurred among children and adults under 40.

Humans have little pre-existing natural immunity to the H5N1 virus infection. If H5N1 viruses gain the ability for efficient and sustained transmission among humans, an influenza pandemic could result with potentially high rates of illness and death worldwide.

To attack this problem, Dr. Alexander “Sasha” Kabanov, Ph.D., D.Sc., has recruited researchers from the fields of microbiology, biochemistry, virology, immunology, materials science and engineering.

ISU experts in biomaterials for drugs, vaccines and gene delivery, tissue engineering and veterinary microbiology collaborate with UNMC experts in polymer chemistry, biosecurity, microbiology and aerosol vaccination techniques.

Dr. Kabanov hopes to adopt platforms to develop vaccines for other respiratory infections such as pulmonary tularemia, which the U.S. government classifies as a Class A agent, meaning it has the potential to pose a severe threat to public health and safety.

Last year, the project was expanded to develop a vaccine against such disorders of the central nervous system (CNS) as Parkinson’s disease, which can develop naturally through either environmental or genetic factors or through exposure to chemical weapons. This portion of the project is led by Howard Gendelman, M.D., the Larson Professor of Internal Medicine and Infectious Diseases, chairman of the department of pharmacology and experimental neuroscience and director of the Center for Neurovirology and

Neurodegenerative Disorders (CNND) at UNMC.

He will evaluate the three nanotechnology platforms to determine which improves protection, defends the brain against the disease and reduces toxicity to the body. Dr. Gendelman said human studies are being conducted at the University of Alabama-Birmingham and at UNMC to see if the immune deficits seen in mice also are present in humans with Parkinson’s disease.

The cause of Parkinson’s disease — which affects more than 4 million people worldwide — is the loss of neurons that produce dopamine, a nerve signaling chemical that controls movement and balance.

Neurodegeneration occurs when a normal protein called alpha synuclein clumps, changes shape, then accumulates in the brain. This results in the body attacking it through inflammation and causing destruction of dopamine-producing nerve cells.

UNMC researchers reversed the neurodegenerative effects of alpha synuclein by changing immune responses to it.

In mice with an experimental form of Parkinson’s disease, researchers found that the vaccine enabled T cells to migrate to the damaged area of the brain and trigger a neuroprotective response that reduced disease-linked reactions in the brain. T cells are white blood cells that are key to the immune response. They act like soldiers who search out and destroy targeted invaders. 