MedicalXpress

As Zika rages, scientists step up antiviral drug research

February 12 2016, by Jonel Aleccia, The Seattle Times

Samples of Zika virus from the outbreak raging across Brazil and Latin America arrived at the University of Washington last month, where they were quickly locked in a biosafety freezer, awaiting research aimed at stopping the germ tied to growing numbers of devastating birth defects.

The surge of the mosquito-borne virushas lent new urgency to early tests of a small, druglike molecule that one day may thwart not only that virus, but also the next threat that explodes across the globe, said Michael Gale Jr., the UW immunologist leading the work.

"It caused us to change our priorities," said Gale, director of the UW Center for Innate Immunity and Immune Disease.

He is working with Kineta, the Seattle biotech firm he co-founded, and scientists at the University of Texas at Galveston to create what could become a broad-spectrum antiviral drug to treat so-called RNA viruses. Those include not only Zika, but other bad bugs that cause infection and disease: West Nile, Nipah, Lassa and Ebola - plus hepatitis C and type-A influenza.

Currently, there are no broad-spectrum antiviral drugs and few cures or even treatments for RNA viruses.

The local scientists see promise in KIN1400, the small molecule that triggers an innate immune response inside cells, launching a cascade of effects that overwhelm the viruses, preventing them from replicating.

"The hope is to develop a pan-viral drug that would not have to be rejiggered to a specific virus," said Shawn Iadonato, Kineta's chief scientific officer.

A study by Gale and his team published in the Journal of Virology in December showed that KIN1400 reduced viral load in cells infected with several types of viruses and jump-started the immune response. Unpublished studies indicate the molecule halted a 10-times lethal dose of H1N1 flu in mice and protected against dengue and other germs, researchers said.

"One way to describe it is that the body's antiviral program is getting switched on," Iadonato said.

Triggering a reaction that stimulates the host's response, instead of targeting the virus itself, helps eliminate one of the most challenging aspects of RNA viruses: their ability to mutate and evade the immune system.

Because such viruses are so wily, they're the cause of emerging and re-emerging outbreaks like those seen with West Nile, dengue, chikungunya and Ebola, said Eramian.

The December paper didn't mention Zika virus, but researchers say they decided to speed up tests after it was clear the mosquito-borne virus was spreading rapidly. Originally detected in Africa nearly 70 years ago, Zika has now spread to more than 25 countries. Adding to the urgency is a suspected link between Zika virus infections and the birth defect microcephaly, which has been reported in more than 4,700 pregnant women in Brazil. The disorder can cause severe brain damage, leading to intellectual and physical problems.

It's far too early to call KIN1400 a "cure" for Zika or any other RNA

virus. But the Seattle scientists say the research shows clear promise for suppressing and controlling viral infection for those already diagnosed.

For now, Gale and his colleagues appear to be the only local researchers actively investigating Zika. Jennifer Dent, president of Seattle's BIO Ventures for Global Health (BVGH), which tracks such research, said she wasn't aware of area projects involving the virus. However, other scientists and firms in the U.S. and around the world are now fast-tracking investigations into potential vaccines to prevent Zika infections and drugs to treat them.

A broad-spectrum antiviral drug is something of a holy grail for infectious-disease experts pondering Zika and other threats, said Dr. William Schaffner, a professor of preventive medicine at Vanderbilt University in Nashville, Tenn.

"If you're talking about my wish list, the first two things I would wish for, clearly, are a more precise diagnostic test and a safe and effective vaccine," he said. "Third on my list would be a therapeutic agent like this, especially one that one might employ during pregnancy."

Gale and his colleagues are waiting for UW officials to approve the final protocols to allow testing of the newly acquired Zika virus samples to begin, he said.

Next steps will be to develop accurate dosing levels and to test the compound in larger animals and in humans, a process that could take between two and five years.

"A lot of the work we're trying to do right now is to make sure that we're not caught flat-footed when the next global crisis arises," Iadonato said.