

In the news

RESURRECTION OF A POXVIRUS CAUSES ALARM

The global eradication of smallpox is widely regarded as one of the greatest triumphs of public health. Vaccination against variola virus (the cause of smallpox) ended in the 1980s, and most people today have no immunity to the virus, raising concerns over its accidental or deliberate reintroduction to the population. A highly controversial study in which researchers generated an infectious horsepox virus (an extinct poxvirus that is related to variola virus) using synthetic DNA and reverse genetics was recently reported (*PLOS ONE*, 19 Jan 2018), causing alarm in the scientific community because its methods could be used to construct other, more dangerous poxviruses.

In collaboration with Seth Lederman at Tonix Pharmaceuticals, United States, David Evans and his Research Associate Ryan Noyce at the University of Alberta, Canada, ordered 10 large fragments of synthetic DNA that were based on the horsepox virus genome, along with two short vaccinia virus (the smallpox vaccine) terminal sequences that were then used to construct a chimeric horsepox virus molecular clone. This clone generated infectious virus when it was introduced into cells that were infected with a helper virus — Shope fibroma virus. The researchers state that this is the first time a poxvirus was generated using synthetic biology techniques.

The researchers assert that this is an important advance in the development of a safer vaccine against smallpox. They believe that the modern vaccine has evolved to replicate better in humans since it was first isolated by Edward Jenner ~200 years ago, explaining adverse reactions such as encephalitis, myopericarditis and rashes. The team believe that there is firm evidence that Jenner's vaccine is derived from a horsepox virus that transmitted to cows rather than from a cowpox virus, contrary to common belief. Horsepox virus may therefore provide a safer vaccine alternative as the virus more closely resembles the original vaccine that was isolated by Jenner, they hypothesize. Further investigation is required to determine whether horsepox virus is safer than vaccinia virus in humans, but the team found that the virus protected mice from a lethal virus challenge. Nevertheless, the need for a safer smallpox vaccine has been called into question (*Science*, 19 Jan 2018), as Modified Vaccinia Ankara (MVA) has been developed as an alternative and was found to be safe in immunocompromised individuals.

The PLOS Dual Use Research of Concern Committee “unanimously agreed that on this occasion, the benefits of publication outweigh the risks.” “The study did not provide new information specifically enabling the creation of a smallpox virus, but uses known methods, reagents and knowledge that have previously been used in the synthesis of other viruses,” they concluded (*PLOS ONE*, 19 Jan 2018). However, many scientists do not agree. “If anyone wants to recreate another poxvirus, they now have the instructions to do that in one place,” stated Andreas Nitsche, Robert Koch Institute, Germany (*Science*, 19 Jan 2018).

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