Promising new method for next-generation live-attenuated viral vaccines against Chikungunya virus

February 21 2013

Researchers have successfully applied a novel method of vaccine creation for Chikungunya virus (CHIKV) using a technique called large scale random codon re-encoding. Using this approach, a group from the UMR_D 190, Emerging viruses Department in Marseille, France in collaboration with the University of Sydney, Australia, demonstrated that the engineered viruses exhibit a stable phenotype with a significantly decreased viral fitness (i.e., replication capacity), making it a new vaccine candidate for this emerging viral disease. This new report publishes on February 21 in the Open Access journal, *PLOS Pathogens*.

There is an immense need for the development of vaccines targeting many emerging viral pathogens. CHIKV has been responsible for several million human cases over the last decade and represents a striking example of a re-emerging, arthropod-borne, human pathogen for which no licensed vaccine exists. Worryingly, one of the vectors of CHIKV, the mosquito Aedes albopictus, has dispersed into new regions (including temperate areas) resulting in outbreaks of this disease where they had never been previously observed, for example in Italy.

Using the large-scale codon re-encoding method, Antoine Nougairede and colleagues were able to synthetically modify the nucleic acid composition of the virus without modifying the encoded viral proteins. When this method was applied to poliovirus and Influenza A virus, it resulted in a live but attenuated virus that had significant reduction of

viral fitness. In contrast with previous studies, which employed a targeted approach of codon re-encoding, this new study demonstrates that a random approach reduced the replicative fitness of CHIKV in both primate and arthropod cells. The employed strategy also prevented the reversion of the attenuated phenotype by mutation or recombination, thus reducing the possibility that the newly created virus strain could evolve back to the pathogenic version.

The findings by Nougairede et al. suggest that large-scale codon re-encoding can provide a strong basis for the rapid design of next-generation viral vaccines against emerging viral pathogens, as soon as their genome sequence has been determined. It represents an exciting route to vaccine development because it intrinsically alleviates the likelihood of novel pathogenic properties of the designed live vaccine, and allows modulation of the amount of reduced fitness by altering the terms and degree of the genetic re-encoding. Thus, this strategy potentially allows for the generic development of live attenuated vaccines against many new viral pathogens, with reduced costs and the potential single dose induction of long-term immunity.

More information: Nougairede A, De Fabritus L, Aubry F, Gould EA, Holmes EC, et al. (2013) Random Codon Re-encoding Induces Stable Reduction of Replicative Fitness of Chikungunya Virus in Primate and Mosquito Cells. PLoS Pathog 9(2): e1003172. doi:10.1371/journal.ppat.1003172

vaccines.html