JOURNAL OF VIROLOGY, July 2008, p. 6782 Vol. 82, No. 13
0022-538X/08/$08.00+0 doi:10.1128/JVI.00370-08

Letter to the Editor

Caution about Newcastle Disease Virus-Based Live Attenuated Vaccine

In several recent papers, two published last year in the Journal of Virology by DiNapoli et al. (3) and Ge et al. (4), an earlier study by Martinez-Sobrido et al. in 2006 (6), and a review by Bukreyev et al. in 2006 (1), Newcastle disease virus (NDV) is proposed as a potential vector in the development of a novel bi- or multivalent vaccine. We question whether those studies satisfactorily address the possibility of genetic exchange involving nonsegmented negative-strand RNA viruses such as NDV.

In fact, powerful evidence of recombination in NDV was first found as early as 2003 (2). Two recent studies (5, 8) further demonstrated recombination events in NDV. In particular, a natural multirecombinant was identified, which shows that the recombination rate might not be low, at least in NDV (5). It has also been found that NDV live attenuated vaccines have the capacity to play roles in shaping NDV evolution by homologous recombination with wild-type virus (5). In addition, there is more and more evidence of homologous recombination involving other nonsegmented negative-strand RNA viruses like Zaire Ebola virus (10), measles virus (9), mumps virus (2), canine distemper virus (7), etc. Unfortunately, neither recombination between a vaccine virus and other circulating nonsegmented negative-strand RNA viruses resulting in untoward recombinants nor potential instability of the inserted foreign gene was fully addressed and evaluated in these studies.

We should never entirely dismiss the possibility of untoward recombination events. Safety issues with respect to the use of NDV-based live attenuated vaccine need to be recognized and addressed. Therefore, coinfection laboratory studies, including in vivo experiments, with vaccine candidate and wild-type viruses should be carried out to better evaluate the risks associated with genetic exchange.

REFERENCES

1. **Bukreyev, A., M. H. Skiadopoulos, B. R. Murphy, and P. L. Collins.** 2006. Nonsegmented negative-strand viruses as vaccine vectors. J. Virol. **80:**10293–10306.
2. **Chare, E. R., E. A. Gould, and E. C. Holmes.** 2003. Phylogenetic analysis reveals a low rate of homologous recombination in negative-sense RNA viruses. J. Gen. Virol. **84:**2691–2703.
3. **DiNapoli, J. M., L. Yang, A. Suguitan, Jr., S. Elankumaran, D. W. Dorward, B. R. Murphy, S. K. Samal, P. L. Collins, and A. Bukreyev.** 2007. Immunization of primates with a Newcastle disease virus-vectored vaccine via the respiratory tract induces a high titer of serum neutralizing antibodies against highly pathogenic avian influenza virus. J. Virol. **81:**11560–11568.
4. **Ge, J., G. Deng, Z. Wen, G. Tian, Y. Wang, J. Shi, X. Wang, Y. Li, S. Hu, Y. Jiang, C. Yang, K. Yu, Z. Bu, and H. Chen.** 2007. Newcastle disease virus-based live attenuated vaccine completely protects chickens and mice from lethal challenge of homologous and heterologous H5N1 avian influenza viruses. J. Virol. **81:**150–158.
5. **Han, G., C. He, N. Ding, and L. Ma.** 2008. Identification of a natural multi-recombinant of Newcastle disease virus. Virology **371:**54–60.
6. **Martinez-Sobrido, L., N. Gitiban, A. Fernandez-Sesma, J. Cros, S. E. Mertz, N. A. Jewell, S. Hammond, E. Flano, R. K. Durbin, A. García-Sastre, and J. E. Durbin.** 2006. Protection against respiratory syncytial virus by a recombinant Newcastle disease virus vector. J. Virol. **80:**1130–1139.
7. **McCarthy, A. J., M. A. Shaw, and S. J. Goodman.** 2007. Pathogen evolution and disease emergence in carnivores. Proc. Biol. Sci. **274:**3165–3174.
8. **Qin, Z., L. Sun, B. Ma, Z. Cui, Y. Zhu, Y. Kitamura, and W. Liu.** 2008. F gene recombination between genotype II and VII Newcastle disease virus. Virus Res. **131:**299–303.
9. **Schierup, M. H., C. H. Mordhorst, C. P. Muller, and L. S. Christensen.** 2005. Evidence of recombination among early-vaccination era measles virus strains. BMC Evol. Biol. **5:**52–59.
10. **Wittmann, T. J., R. Biek, A. Hassanin, P. Rouquet, P. Reed, P. Yaba, X. Pourrut, L. A. Real, J.-P. Gonzalez, and E. M. Leroy.** 2007. Isolates of Zaire ebolavirus from wild apes reveal genetic lineage and recombinants. Proc. Natl. Acad. Sci. USA **104:**17123–17127.

Guan-Zhu Han*
Xi-Ping Liu
College of Life Science
Shandong Normal University
Jinan, Shandong 250014, China

Si-Shen Li
National Key Laboratory of Crop Biology
College of Agronomy
Shandong Agricultural University
Tai'an, Shandong 271018, China

*Phone: 86-531-86184069
Fax: 86-538-8242226
E-mail: hanguanzhu@yahoo.com