SUMMARY

Title	Research and discovery of innovative ways to treat and prevent influenza (vaccine)
Investigators	Yoshihiro Kawaoka, Professor Makoto Yamashita, Project Professor Division of Virology, Institute of Medical Science, The University of Tokyo
Abstract	Influenza is a serious, often debilitating respiratory illness that can cause complications that lead to hospitalization and death, especially in elderly individuals. Two countermeasures, vaccination and treatment with antivirals, are available to control human influenza. The efficacy of the current influenza vaccines remains inadequate. Given that the targets of all currently approved antivirals are viral proteins, the spread of drug-resistant viruses is a great concern. To control influenza, new measures to increase vaccine efficacy and develop drugs with a low propensity to generate resistant mutants are needed. To increase vaccine efficacy, we aim to establish a high-yield vaccine production system using culture cells. To that end, we will combine cell lines with a high ability to produce virus with viruses of high replicative ability. Cell lines that knockdown a particular host gene, the lack of which promotes virus proliferation in the cells, are being established, and viruses with high replicative ability have been selected from viruses with randomly induced mutations.
Applications	Influenza prophylaxis
Advantages	• More effective vaccine • Fast production of vaccine to combat pandemic influenza
Market Overview	• Annually about 25 million people receiving influenza vaccination in Japan • About 6.5 billion Japanese yen spent for influenza vaccination in Japan
Stage of Development	• Preclinical • Find a company to develop the cell-based vaccine and then conduct

	the necessary research experiments as determined in discussions with the company.
Patent Information Publication	• Watanabe et al., Cell Host Microbe 2014, 16:795 • Ping et al., Nat Commun 2015, DOI:10.1038/ncomms9148 • Ping et al., Proc Natl Acad Sci 2016, 113:E8296
Business Opportunity	• Find a company to develop the cell-based vaccine. • Licensing • University: Implementation of the necessary research experiments as determined in discussions with the company. Company: GMP production of the vaccine and clinical trials including safety studies.
Contact to	Division of Virology, Institute of Medical Science, The University of Tokyo Yoshihiro Kawaoka, D.V.M. Ph.D. Tel: 03-5449-5504 e-mail: yoshihiro.kawaoka@wisc.edu Makoto Yamashita, Ph.D. Tel: 03-6409-2207 e-mail: yamakoto@ims.u-tokyo.ac.jp

Appendix

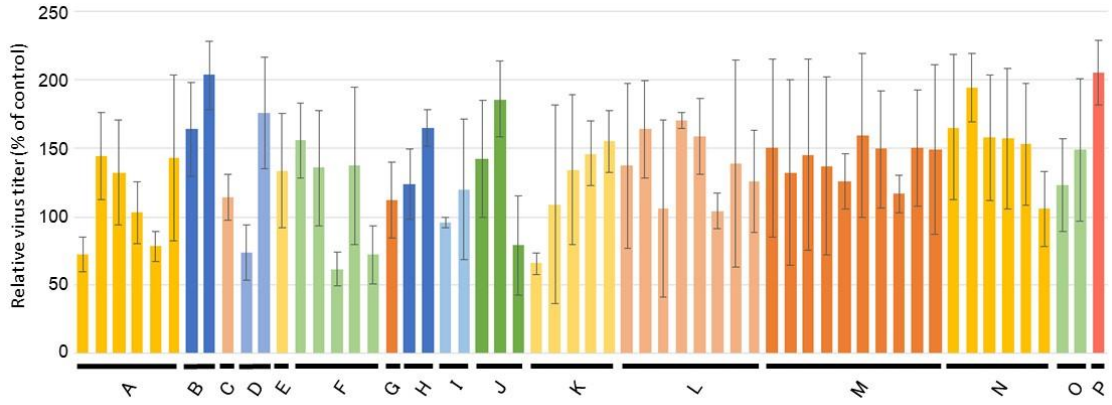

Figure 1. Effects of gene knockout on virus proliferation in cells

Cells, in which a gene (A through P) was knocked out by using the CRISPR/Cas9 method, were infected with influenza virus, and virus titers in the culture supernatant were determined. Relative virus titers are shown. Each bar represents a clone of the gene knocked out cells.

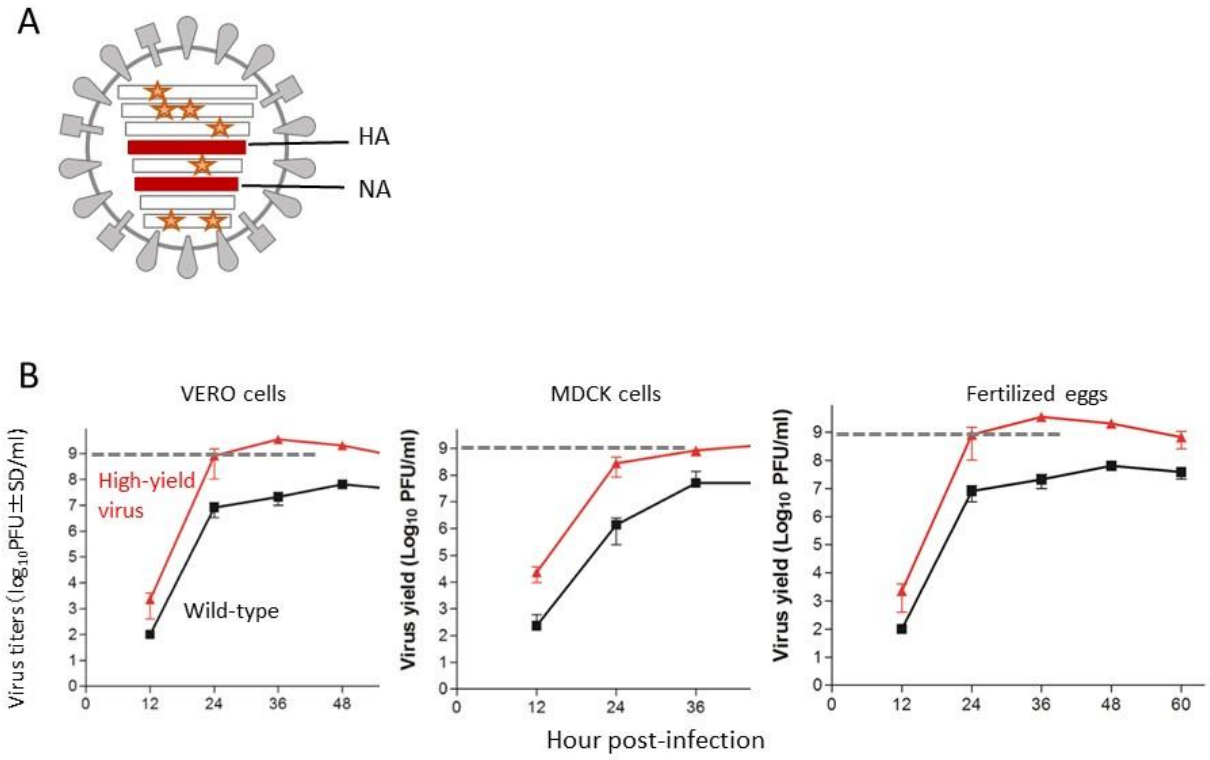

Figure 2. Proliferation of a high-yield virus possessing the HA and NA genes of a different virus

Mutations in the high-yield influenza virus are indicated by ★ (A). Using the backbone of the virus, a high-yield virus possessing the HA and NA genes of an H7N9 virus was generated by using the reverse genetics method. Proliferation of the high-yield virus in Vero cells, MDCK cells, and fertilized eggs was monitored (B).