SUMMARY

Title	Research and discovery of innovative ways to treat and prevent influenza（monoclonal antibody）
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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. Many broadly reactive monoclonal antibodies against the hemagglutinin (HA) stem region of influenza virus have been developed as influenza therapeutic drugs. We established broadly reactive monoclonal antibodies from vaccinated humans, one of which reacted with 18 subtypes of HA, and protected mice from lethal infection with viruses circulating in humans, such as H1N1pdm09, H3N2, H5N1, and H7N9 viruses. Uniquely, this antibody recognized the HA2 helix A in the HA stem, and inhibited virus particle release from infected cells, in contrast to other typical antibodies which neutralize virus by inhibiting membrane fusion steps.
Applications	• Influenza treatment using antibodies.
Advantages	• Effective against viruses resistant to current influenza drugs, newly emerging viruses, and patients with severe influenza.
Market Overview Japan	• Overall about 150 million people suffering from influenza viruses annually • About 3–3.5 billion Japanese yen, depending on the size of the epidemic.

Stage of Development	• Preclinical • Find a company to further develop this antibody for influenza treatment, and conduct the necessary research experiments as determined in discussions with the company.
Patent Information	• PCT/JP2017/029911 (2017/8/22)
Publication	• EBioMedicine 17 (2017) 182–191
Business Opportunity	• Find a company to develop the antibody. • Exclusive licensing • University: Implementation of the necessary research experiments as determined in discussions with the company. Company: GMP production of the antibody and clinical trials including safety studies.
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Appendix

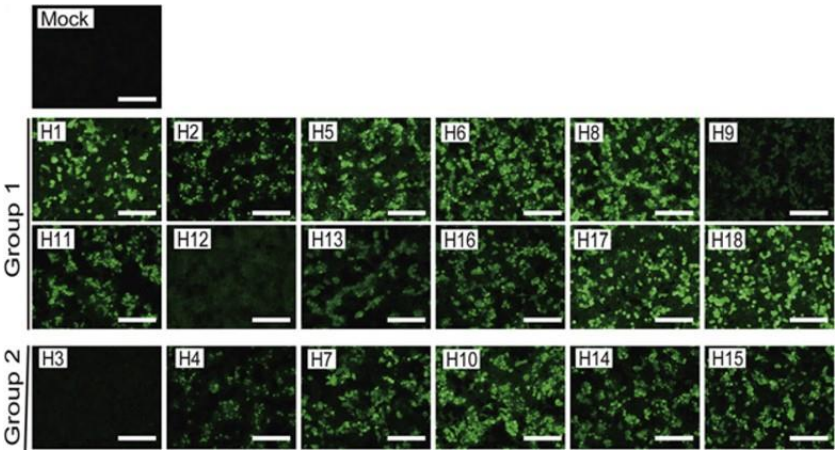

Figure 1. Binding of the monoclonal antibody to the H1- through H18-HA subtypes

293T cells were mock-transfected or transfected with plasmids encoding the H1- to H18-HA subtypes. Expressed HAs were detected by the monoclonal antibody, followed by anti-human IgG conjugated with Alexa Fluor 488. Scale bars, 100 μm. H3-HA was not detected by the monoclonal antibody in this assay but binding to H3-HA was detected by means of bio-layer interferometry.

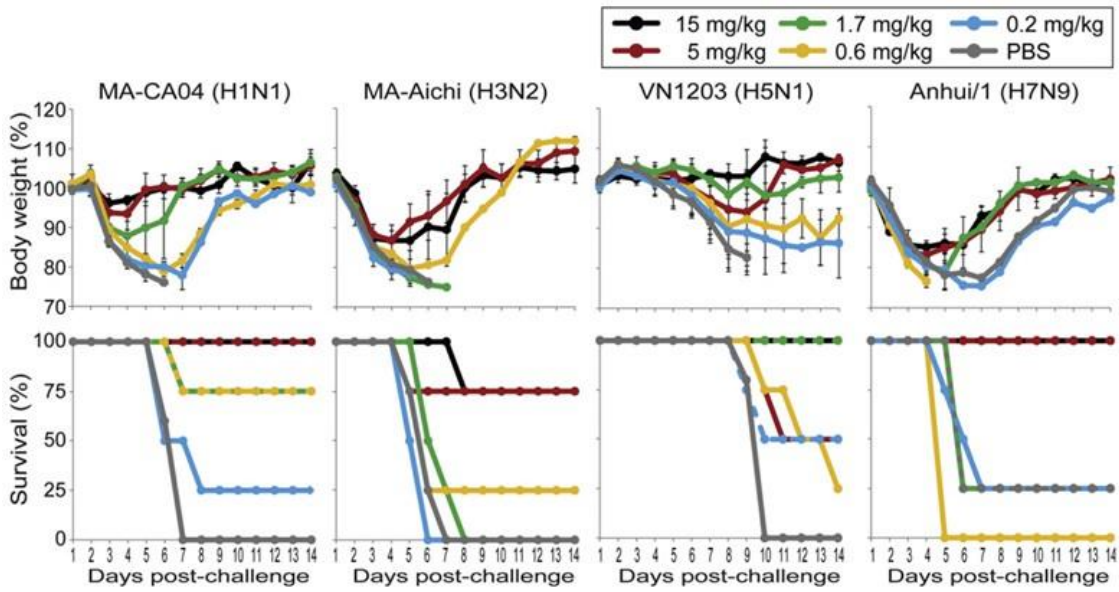

Figure 2. Protection of mice from lethal infection with various influenza viruses

The monoclonal antibody was intraperitoneally injected at the indicated doses. One day later, the mice were challenged with 10 MLD_{50} of mouse-adapted (MA)-CA04 (H1N1pdm09), MA-Aichi (H3N2), VN1203 (H5N1), or Anhui/1 (H7N9) virus. Body weight (upper) and survival (lower) were monitored daily for 14 days. Mouse body weights are expressed as the mean ± SD.