Yeast display platform technology to prepare oral vaccine against lethal H7N9 virus challenge in mice

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S.cerevisiae EBY100/pYD5-HA, Yeast display technology, Influenza A pandemic

Abstract

Background Existing methods for preparing influenza vaccines pose the greatest challenge against the threat of highly pandemic avian influenza virus H7N9 outbreak in the poultry and human. Exploring a new strategy for manufacturing and delivering a safe and effective H7N9 vaccine is urgently needed.

Results An alternative approach, proposed here, is to develop influenza an oral H7N9 vaccine based on yeast display technology in a timely manner. Hemagglutinin (HA) of A/Anhui/1/2013 (AH-H7N9) as a model antigen and characterized its expression on the surface of Saccharomyces cerevisiae (S.cerevisiae) EBY 100. Mice orally administrated with S.cerevisiae EBY100/pYD5-HA produced significant titers of IgG antibody as well as significant amounts of cytokines IFN-γ and IL-4. Importantly, S.cerevisiae EBY100/pYD5-HA could provide complete immune protection against homologous A/Anhui/1/2013 (AH-H7N9) virus challenge.

Conclusion Our findings suggest that platform based on yeast surface technology provides an alternative approach to prepare a promising influenza H7N9 vaccine candidate that can significantly shorten the preparedness period and result in effective protection against influenza A pandemic.

Keywords: S.cerevisiae EBY100/pYD5-HA, Yeast display technology, Influenza A pandemic.

Full-text

Due to technical limitations, full-text HTML conversion of this manuscript could not be completed. However, the manuscript can be downloaded and accessed as a PDF.

Figures

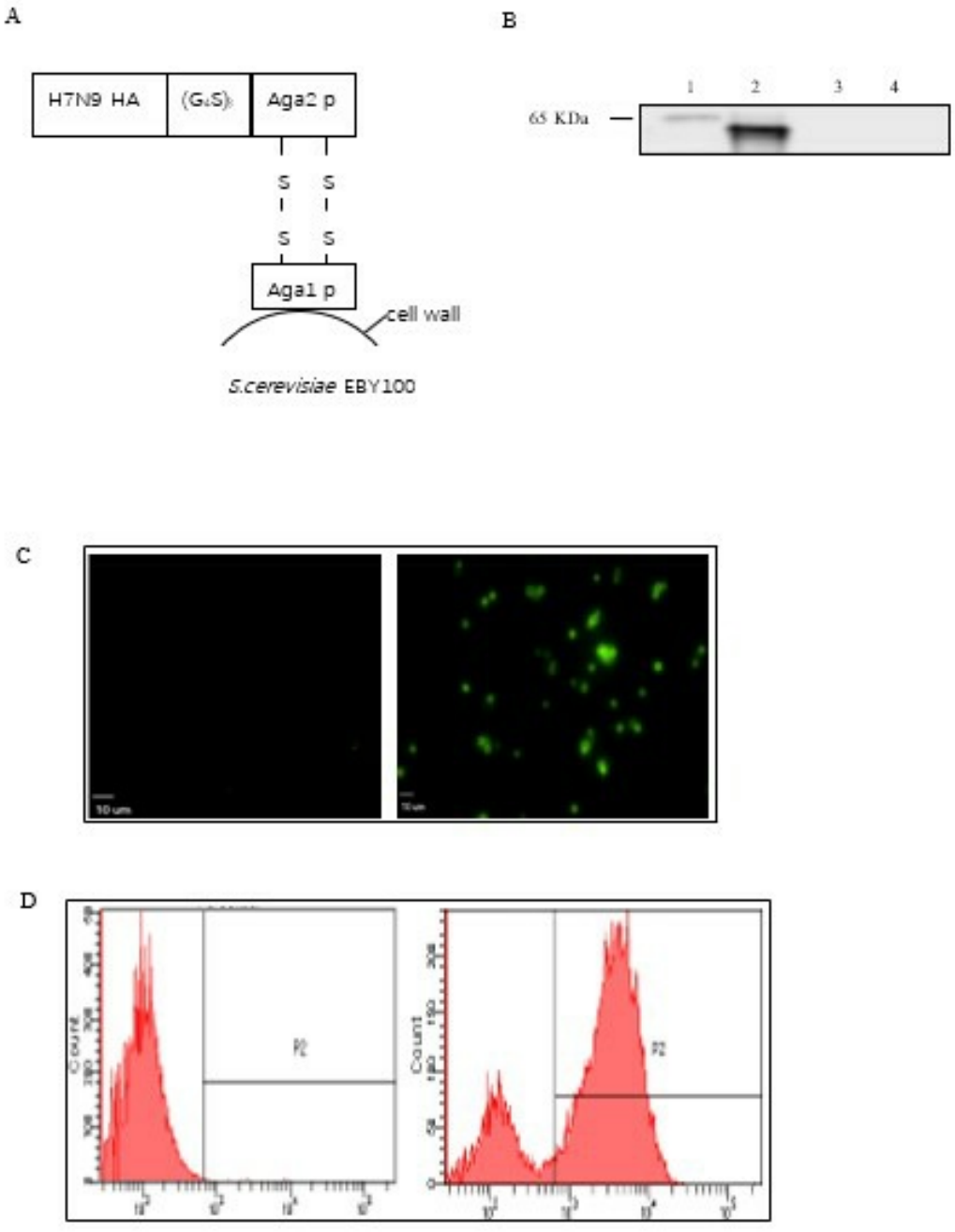
A
H7N9 HA
(G4S)3
Aga2 p
S
S
S
S
Aga1 p
cell wall
S.cerevisiae EBY100
B
1
2
3
4
65 KDa
C
D
P2
P2

Figure 1

Construction of yeast display vector and analysis of the expression of HA protein. (A) 1 Schematic diagram of yeast expression vector (S.cerevisiae EBY100/pYD5-HA) which the displayed 2 protein (HA) was tethered at its C-terminus to Aga2p mating protein through a (G4S)3 linker. (B) Western 3 blotting analysis. Lane 1: HA glycoprotein. Lane 2: Deglycosylation of HA protein. Lane 3: S.cerevisiae 4 EBY100/pYD5 control. Lane 4: Deglycosylation of S.cerevisiae EBY100/pYD5. (C) Immunofluorescence 5 microscope, S.cerevisiae EBY100/pYD5 (left) and S.cerevisiae EBY100/pYD5-HA (right) (magnification 6 400 ×). (D) Flow cytometric analysis, S.cerevisiae EBY100/pYD5 (left) and S.cerevisiae EBY100/pYD5-7 HA (right).

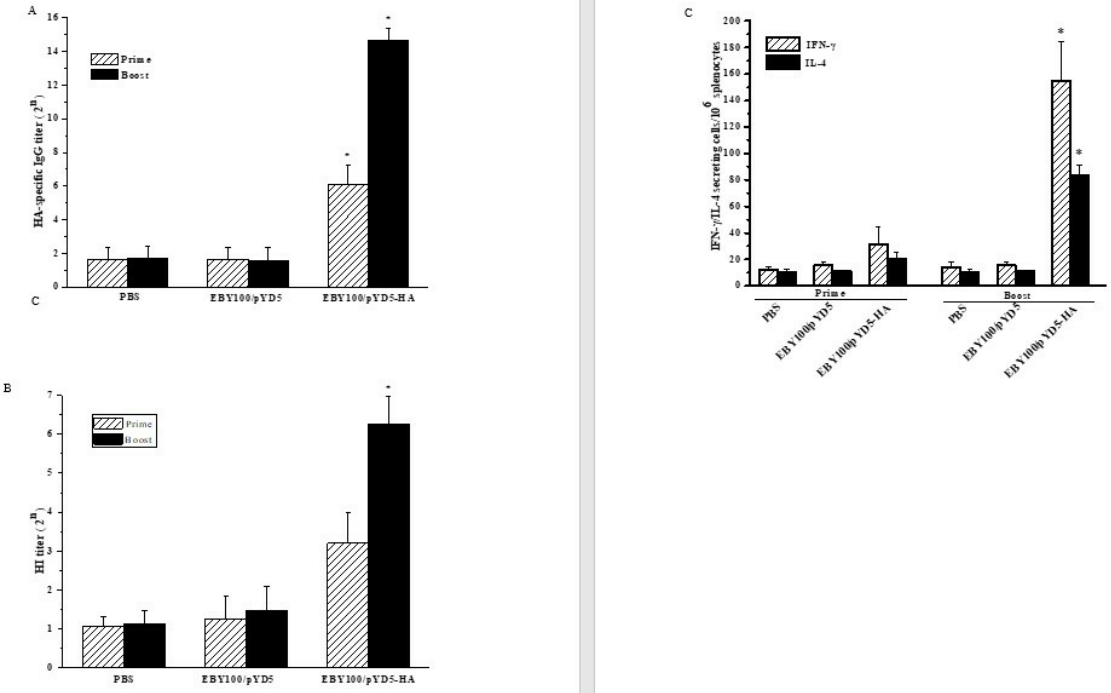

Figure 2

Antibody response detected by ELISA and Hemagglutination inhibition (HI) assay. (A) HA - 10 specific IgG titers. (B) HI titers. (C) The cellular immune responses were assayed by ELISpot assay. 11 Splenocytes derived from vaccination (n=3/group) were incubated on the IFN-γ or IL-4 capture antibody 12 coated with stimulation of HA peptide. IFN-γ and IL-4 spots were counted. The data are presented as mean 13 ± standard deviation (SD). Asterisk indicates statistical significance compared to S.cerevisiae 14 EBY100/pYD5 and PBS groups ($p < 0.05$).

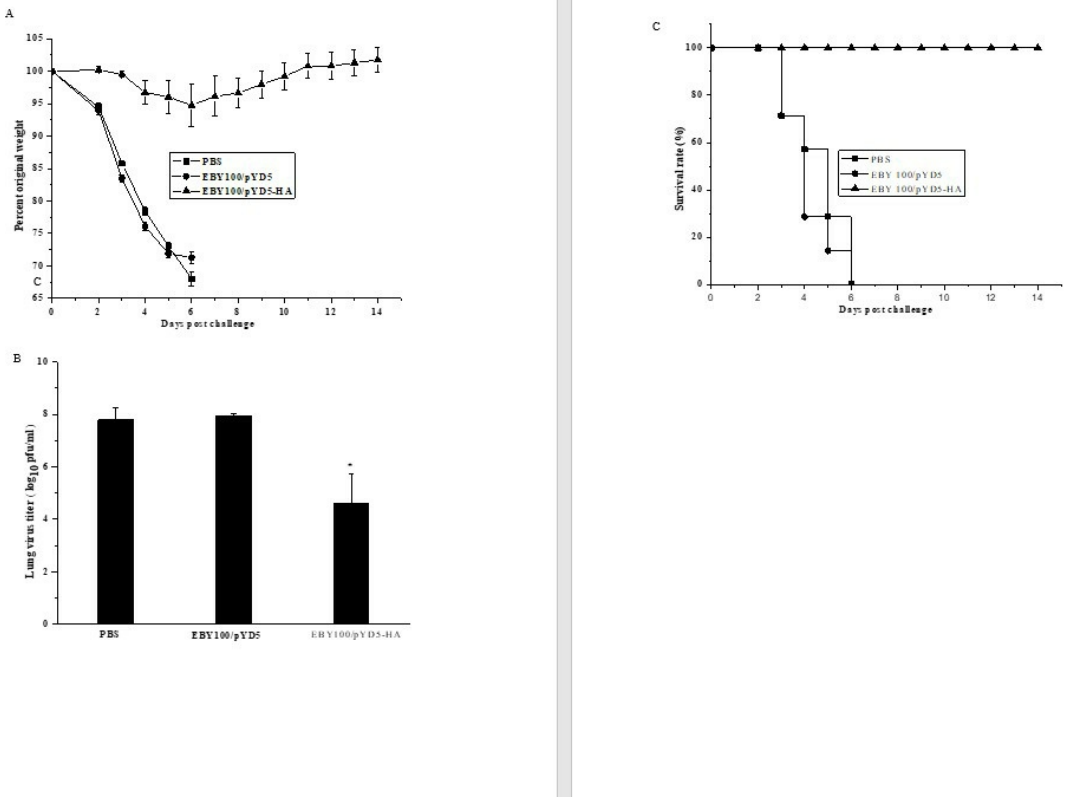

Figure 3

Immune protection conferred by S.cerevisiae EBY100/pYD5-HA against lethal H7N9 virus 18 challenge. Mice were intranasally challenged with a lethal dose (10 × LD50) of A/Anhui/1/2013 (AH-19 H7N9) virus at 2 weeks after the final immunization (n=10/group). (A) Weight change as a percentage. 20 Bars indicate SDs. (B) Lung viral titers were determined by a plaque assay at day 3 after challenge (n=3 of 21 10 challenged mice). (C) Survival rate. Asterisk indicates significant difference compared to S.cerevisiae 22 EBY100/pYD5 and PBS groups ($p < 0.05$).