INTRODUCTION
Influenza epidemics continue to cause morbidity and mortality. Elderly humans over 65 years old constitute up to 90% of all seasonal influenza mortality (1). However, 2009 H1N1 seems to adversely affect young adults (2). Vaccination remains most effective approach to reduce infection (3). Current Inactivated influenza vaccines (IIV) provide protection in healthy young adults with up to 90% efficacy but protection of elderly adults is lower (4). Previous studies report the adjuvant properties of cytokines (5) and chemokines in enhancing efficacy of influenza virus vaccines (6). Studies in our laboratory have demonstrated that influenza A virus bearing chicken-specific immunomodulators enhance seroconversion rates in chicks (7) and influenza virus bearing membrane-bound, mammalian derived immuno-modulatory proteins boosts immunogenicity and protection against lethal challenge in young adult mice (8).

RESULTS
Figure 3: Immunofluorescence cell surface staining of stably transfected MDCK producer cell lines expressing mFlt3L-HA(2C) and mIL12-HA (2D) with MDCK wild type as negative control (A, B).

Figure 4: Inactivated influenza vaccines bearing membrane-bound immunomodulators enhance serum anti-viral antibody titers in aged mice. Serum was collected on day 28 post-boost and antibody titers for influenza virus specific IgG were determined by ELISA. Data is displayed as the mean OD ± SEM (n=5).

Figure 5: CTIV-VAC vaccination significantly reduces viral loads in lung tissue following lethal challenge in young mice. Mice vaccinated with either wild-type vaccine or CTIV-VAC challenged on day 36 post-vaccination with 100 LD₅₀ of mouse-adapted A/PB/34. Mice were sacrificed on day 4 post-challenge and viral loads from homogenized lung tissue (n=5) were determined by tissue culture infectious dose assay. Data is expressed as TCID₅₀ per gram of lung tissue. (*p<0.05, **p<0.01, ***p<0.001 compared to PBS, one way ANOVA)

Figure 6: A/PR/8 bearing mFlt3L-HA retains bioactivity following BPL-inactivation.

Figure 7. Inactivated influenza vaccines bearing membrane-bound immunomodulators protects aged mice against lethal challenge. 14 month old Balb/c mice (N=7) were vaccinated s.c. with 0.375 μg of inactivated A/PR/34 wild type or A/PR/8/B34 bearing membrane-bound IL-2 or IL-4. Mice were boosted with same vaccine and dose on day 21 then challenged with 100 LD₅₀ of mouse-adapted A/PR/8/B34 on day 110 post primary vaccination. PBS served as negative vehicle control. Percent weight change (A) and survival (B) were monitored over time.

CONCLUSION
Membrane-bound Immunomodulatory Influenza Vaccine
- Provide superior protection in both young and aged Balb/c mice against lethal homotypic virus challenge
- Enhance influenza specific IgG antibody titres
- Reduce viral titres in lung tissue following lethal challenge
- Future studies are needed to evaluate optimal single dose of vaccine and mechanisms of CTIV-VAC mediated protection

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REFERENCES