

Protection induced by early stage of vaccination with influenza virus-like particles

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• **Background**

• **We know:**

- **Influenza vaccine takes about 2 - 4 weeks to develop antibodies to protect against influenza virus infection.**
- **Influenza virus-like particle (VLP) is a promising vaccine candidate.**

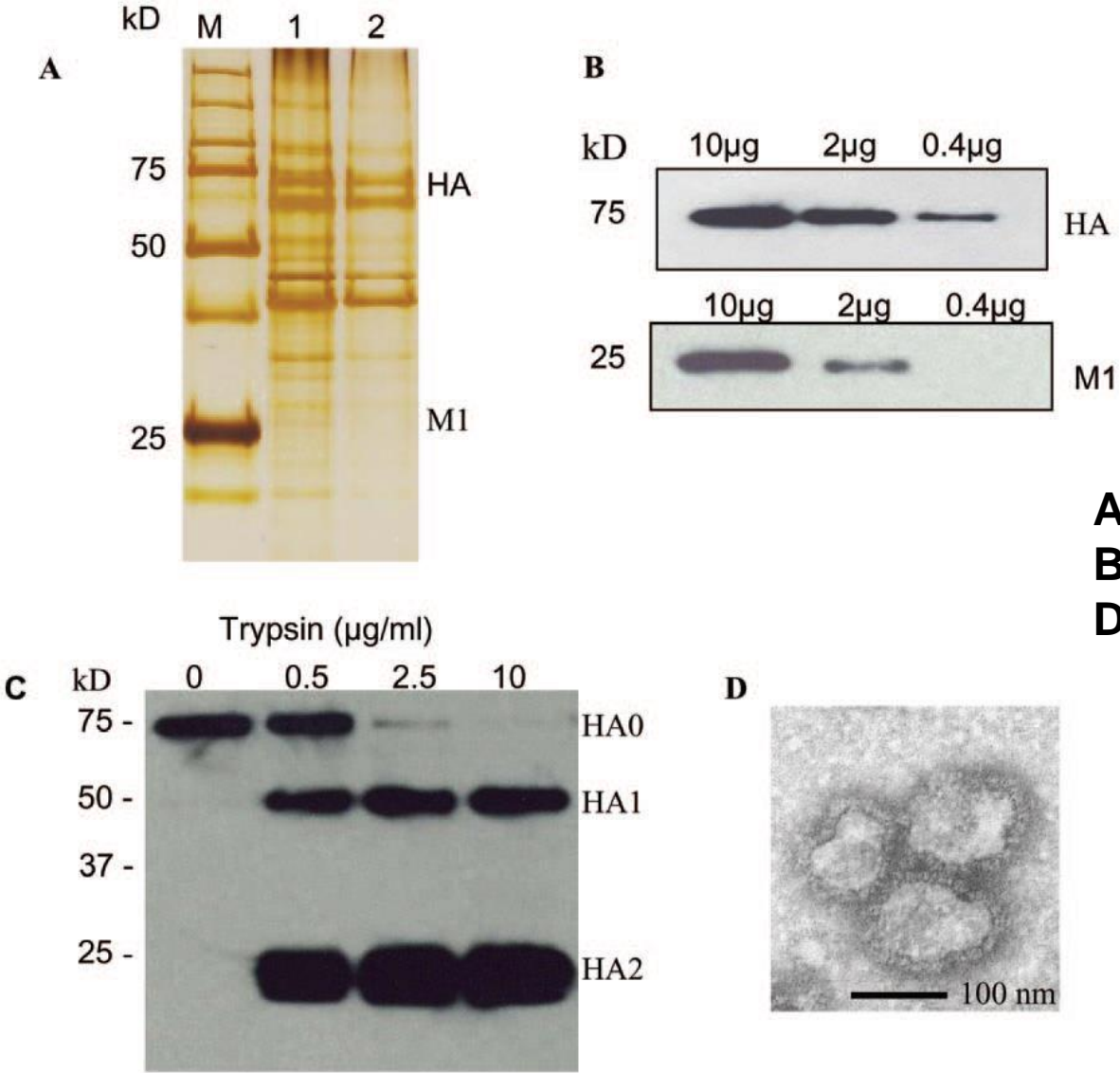
• **We don't know:**

- **Protection (antibody response) induced before 2 weeks post-vaccination**

• **Methods**

- **Vaccine: VLPs (A/California/04/09, hemagglutinin (HA) and M1**
- **Balb/c mice, single immunization (IM, 10 µg of VLPs).**
- **For challenge studies, IN (10 LD50) challenge infections started at very early stage of vaccination**
- **IgG, IgG subtype, ASC in spleen and bone marrow, lung IgG, lung cytokine, lung virus titer, mouse body weight changes and survival**

Fig 1. VLPs characterization



A. Silver stained SDS-PAGE
B, C: Western blot
D. Electron microscopy

Fig 2. Virus-specific total IgG antibody responses

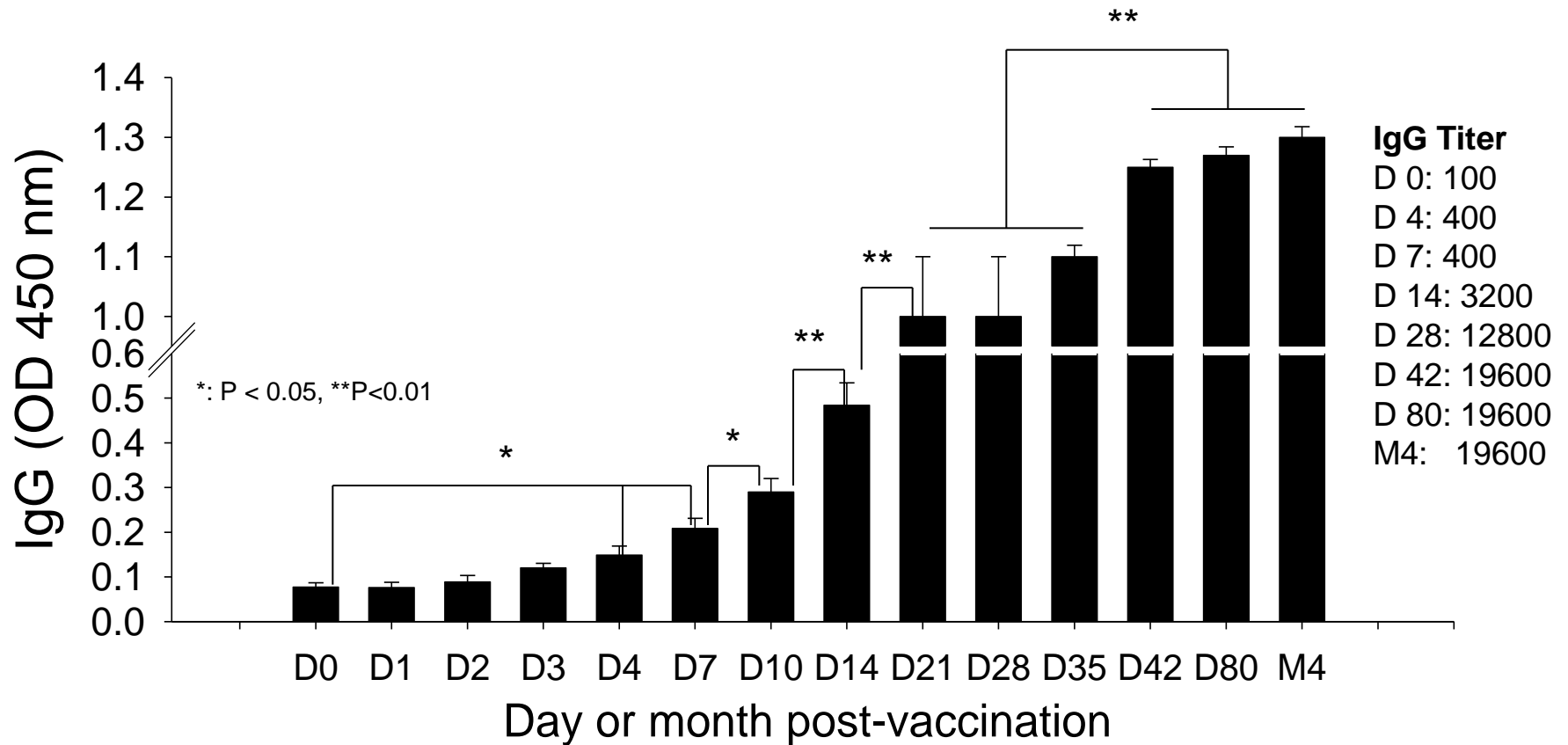


Fig 3. Virus-specific IgG subtype responses

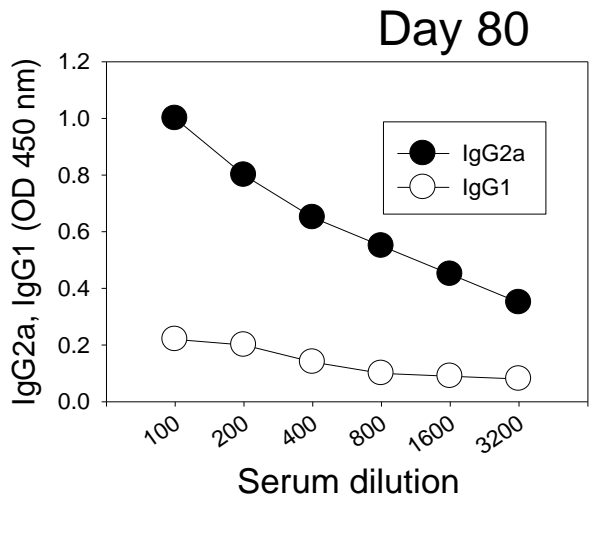
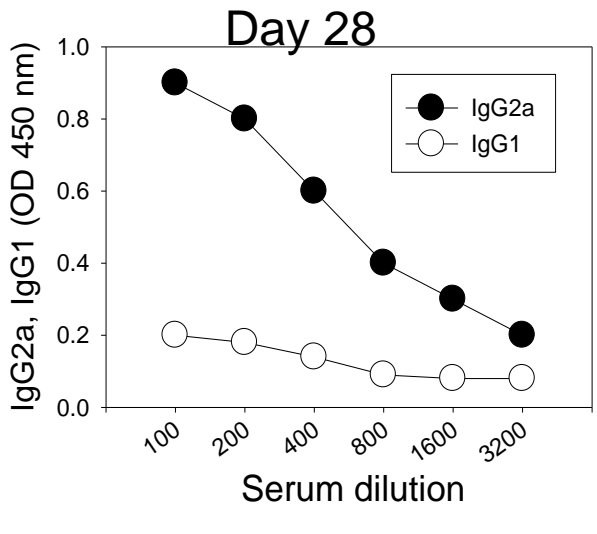
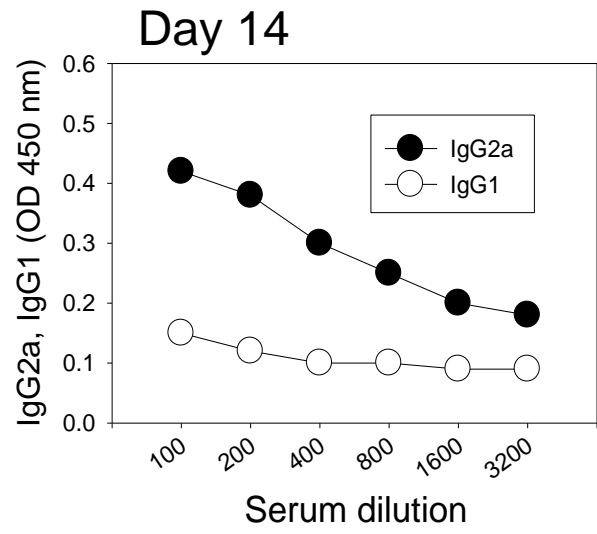
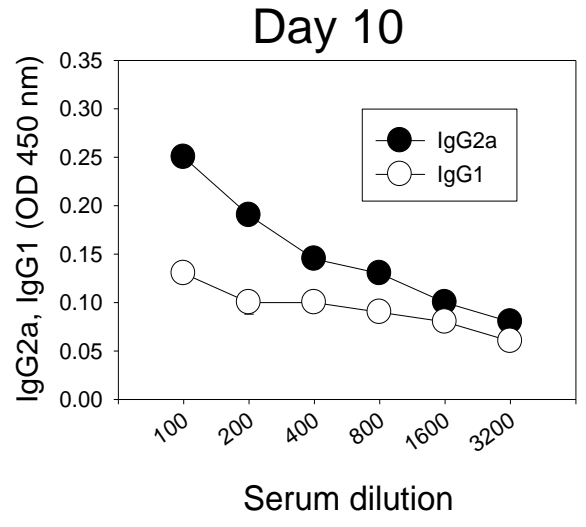
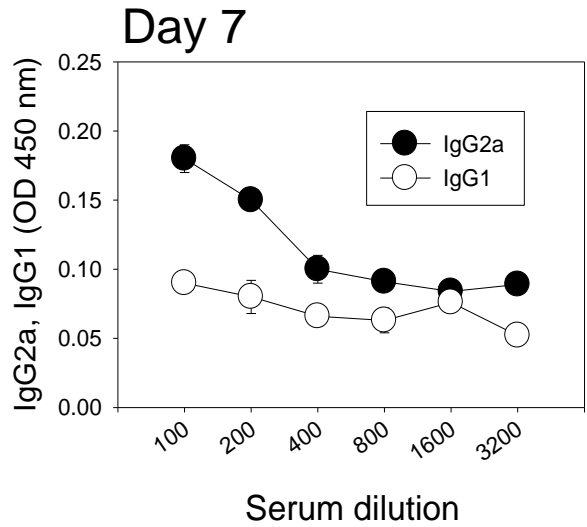
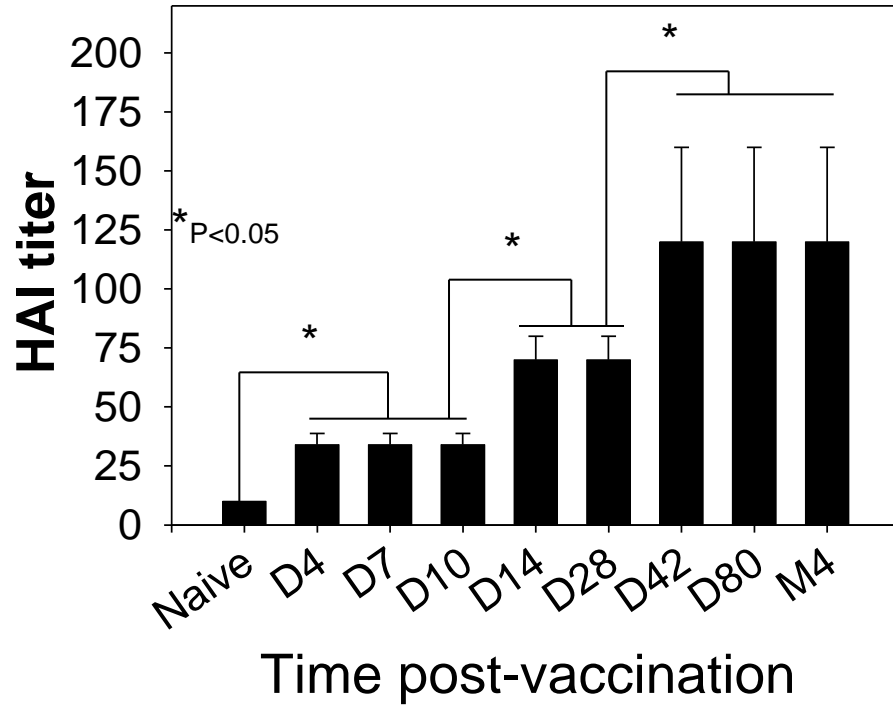


Fig 4. HAI titers at different periods after vaccination

A. HAI titer



B. Neutralizing activity

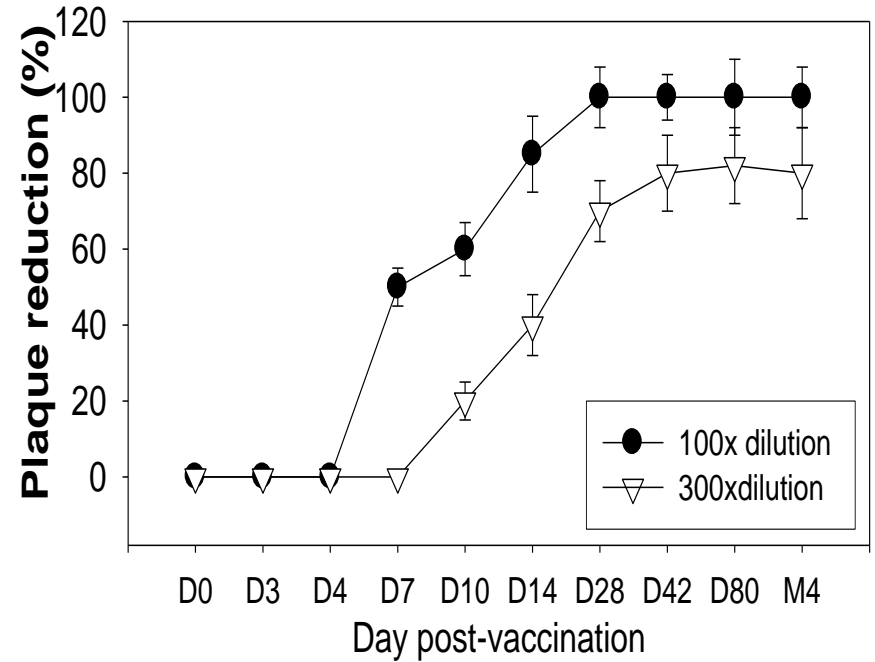


Fig 5. Lung virus titers and survival post-challenge at day 4 and 7 after vaccination

Protection induced by various periods after vaccination

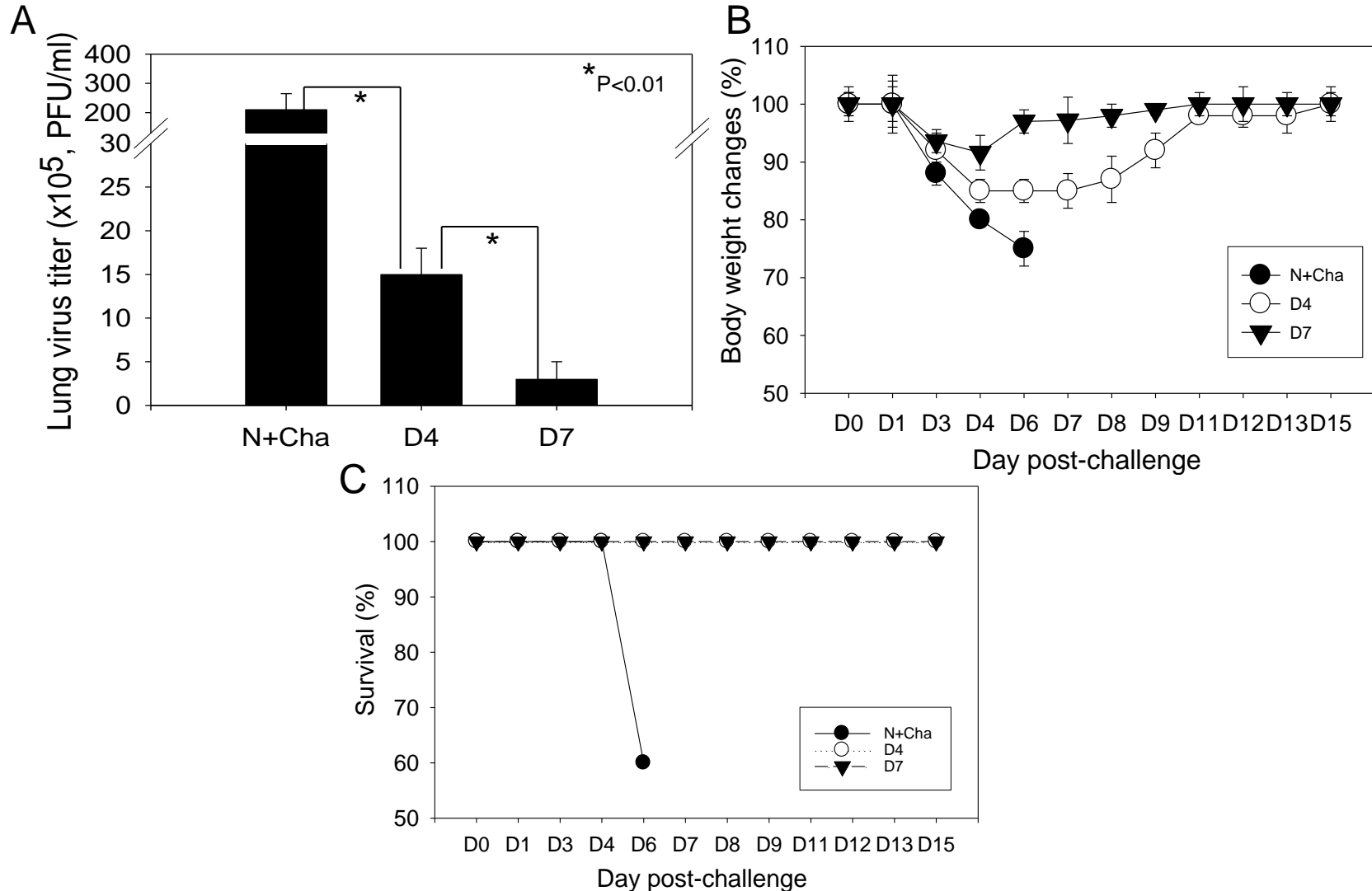


Fig 6. IgG antibody responses in the lung

Antibody secreting cell (ASC) responses

Lung inflammatory cytokine responses

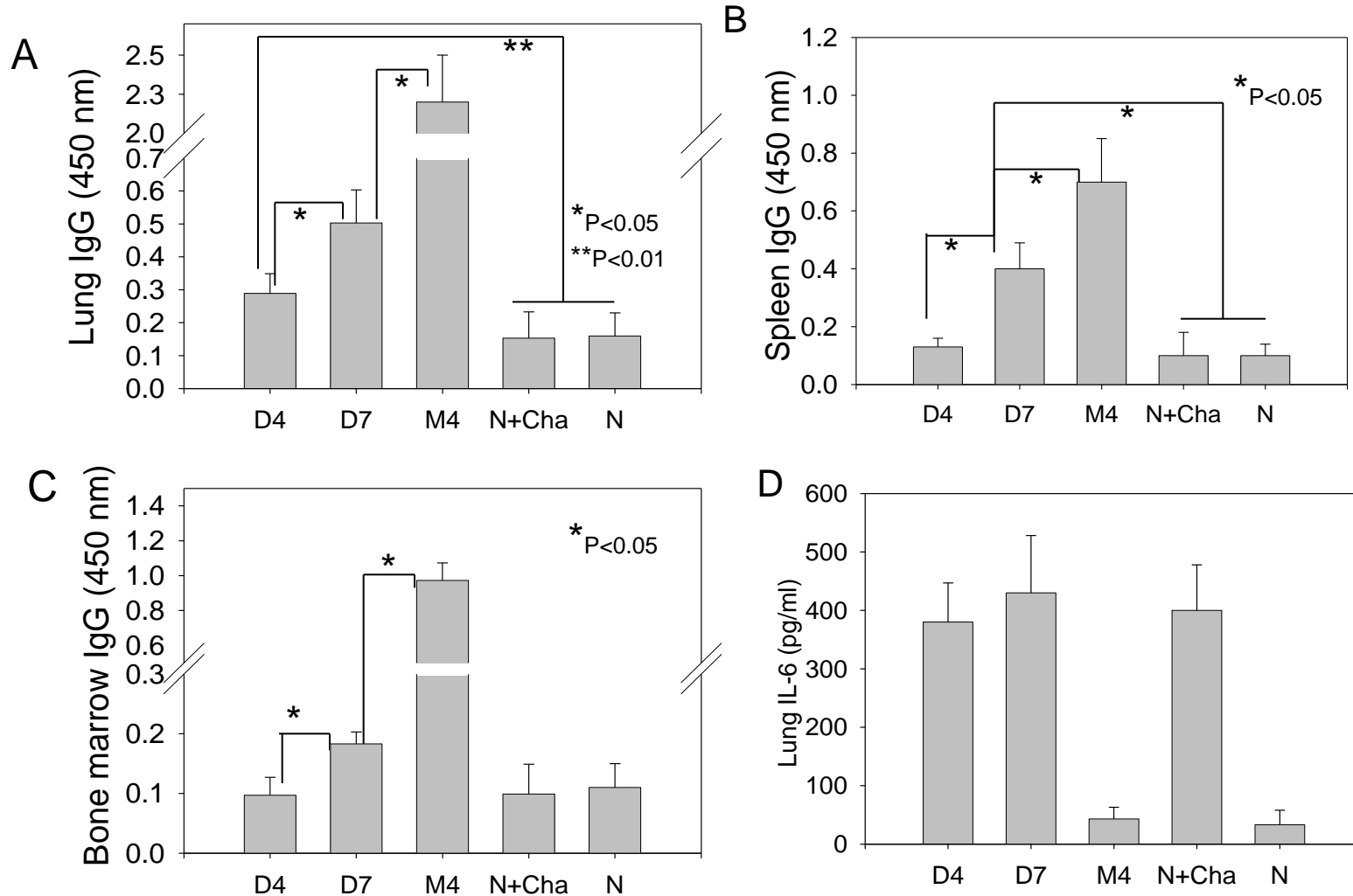


Fig 7. Immune correlates

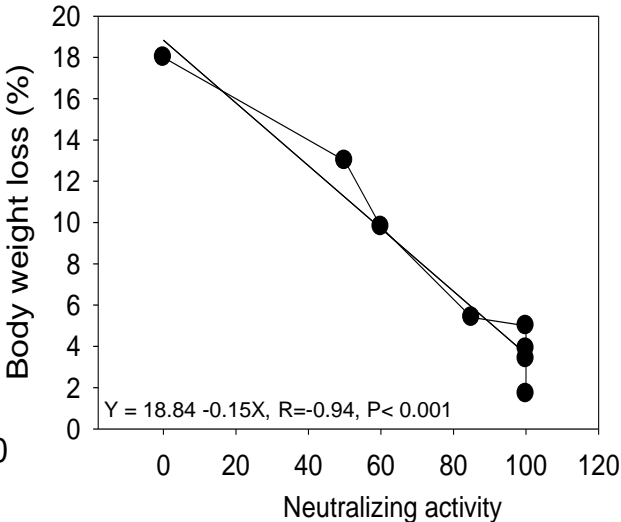
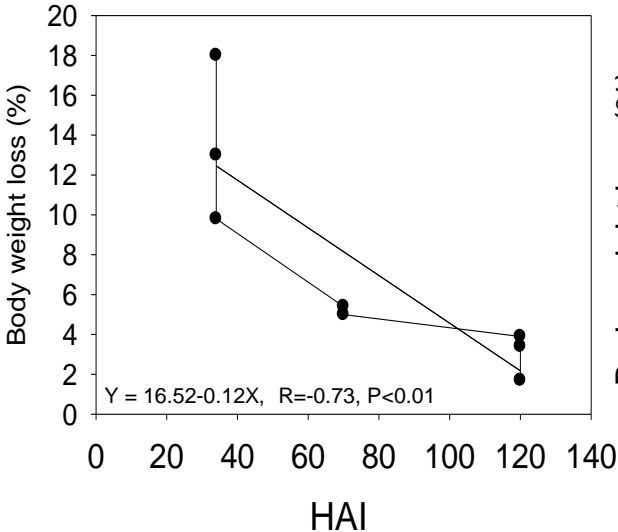
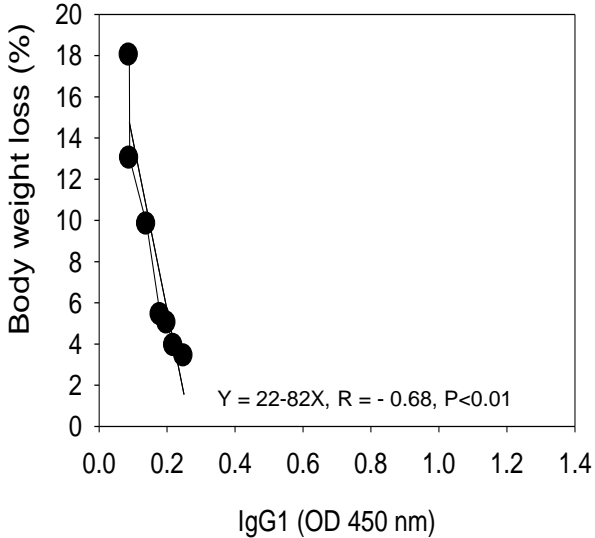
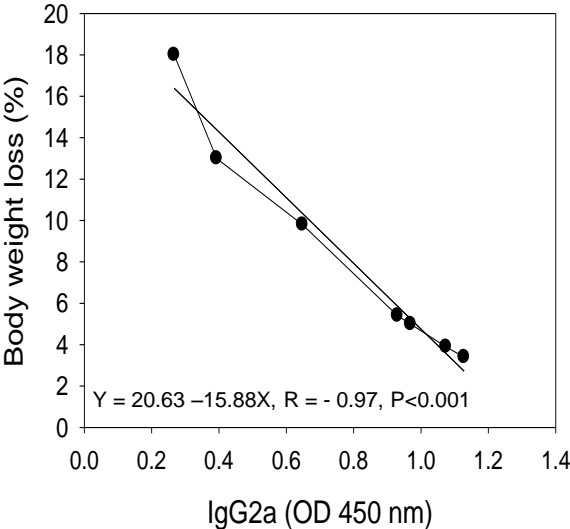
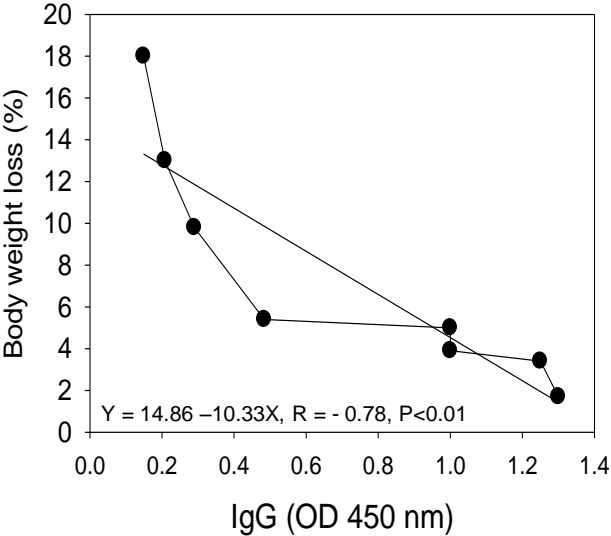


Table1. Immune correlates of protection against pandemic influenza A/California/04/2009

Time post-vaccination	Immune response parameters						
	BW (%)		Survival (%)	IgG (titer)	IgG2a (titer)	HAI	NA
	Day 4	Day 7					
D 0 (Naïve)	14.5	26	0	ND	ND	10	ND
D 1	12.0	22.3	0	ND	ND	10	ND
D 2	15.4	23	0	ND	ND	10-12	ND
D 3	15.0	24.2	0	ND	ND	10-12	ND
D 4	15.0	15.6	100	400	200	32	ND
D 7	10.0	4.4	100	400	400	32	50
D 10	3.5	1.6	100	800	800	40	60
D 14	3.0	0	100	4500	4000	70	80
D 28	2.6	0	100	12800	9000	80	100
D 80	2.0	0	100	19600	12800	100-120	100
Month 4	0.7	0	100	19600	12800	100-120	100

• Conclusion

- VLP vaccination induced significantly higher levels of IgG antibody responses and high HAI titers at day 4 post-vaccination.
- At day 7, predominant IgG2a antibody responses and viral neutralizing antibodies were induced.
- Upon challenge on day 4 and 7 post-vaccination, lung IgG antibody responses and recall IgG antibody-secreting cell responses were induced.
- Lung virus titers decreased significantly at day 7 compared to that at day 4 post-vaccination. The lung virus titer at day 4 post-vaccination also decreased significantly compared to naïve control.
- This study demonstrates that VLP vaccination provides effective protection in the early stage of vaccination.