

Development of Novel Mucosal Adjuvant

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富山から世界へ



富山くすりコンソ

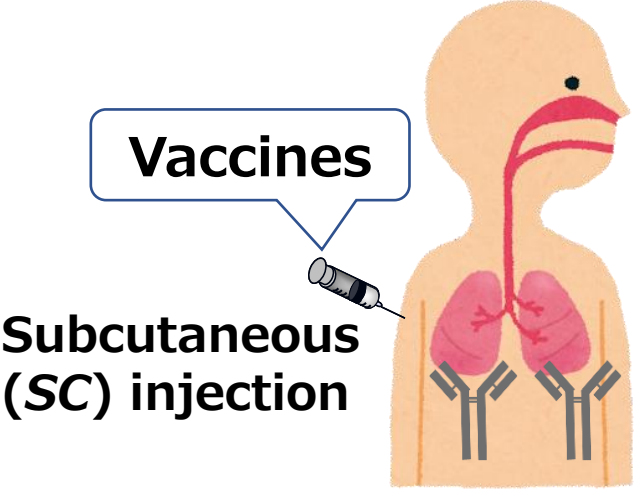
産学官共創プラットフォーム

Objective: Development of a Novel Mucosal Adjuvant for Nasal Vaccines

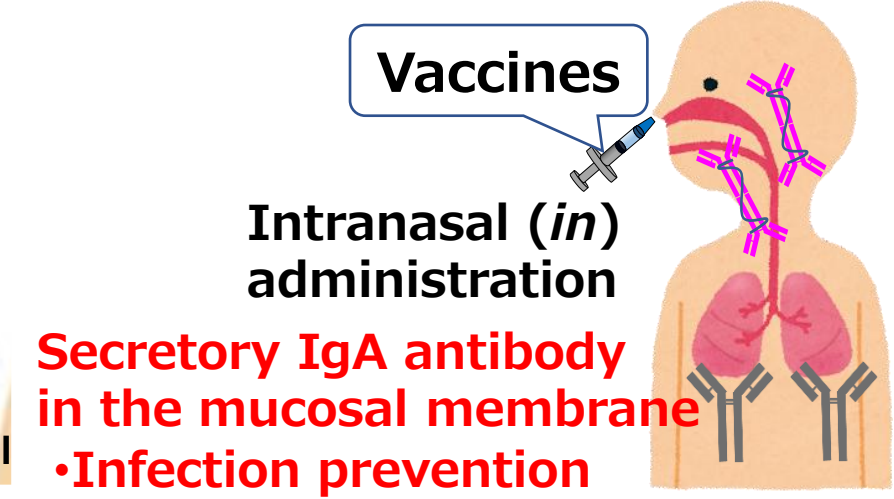
Mucous membranes, which are in constant contact with the outside world, have physical and chemical barrier functions, such as mucociliary movement to eliminate foreign substances and pathogens, making it difficult to induce immune responses.

Useful mucosal adjuvants are necessary for mucosal vaccines to effectively induce mucosal immune responses.

Subcutaneous vaccines

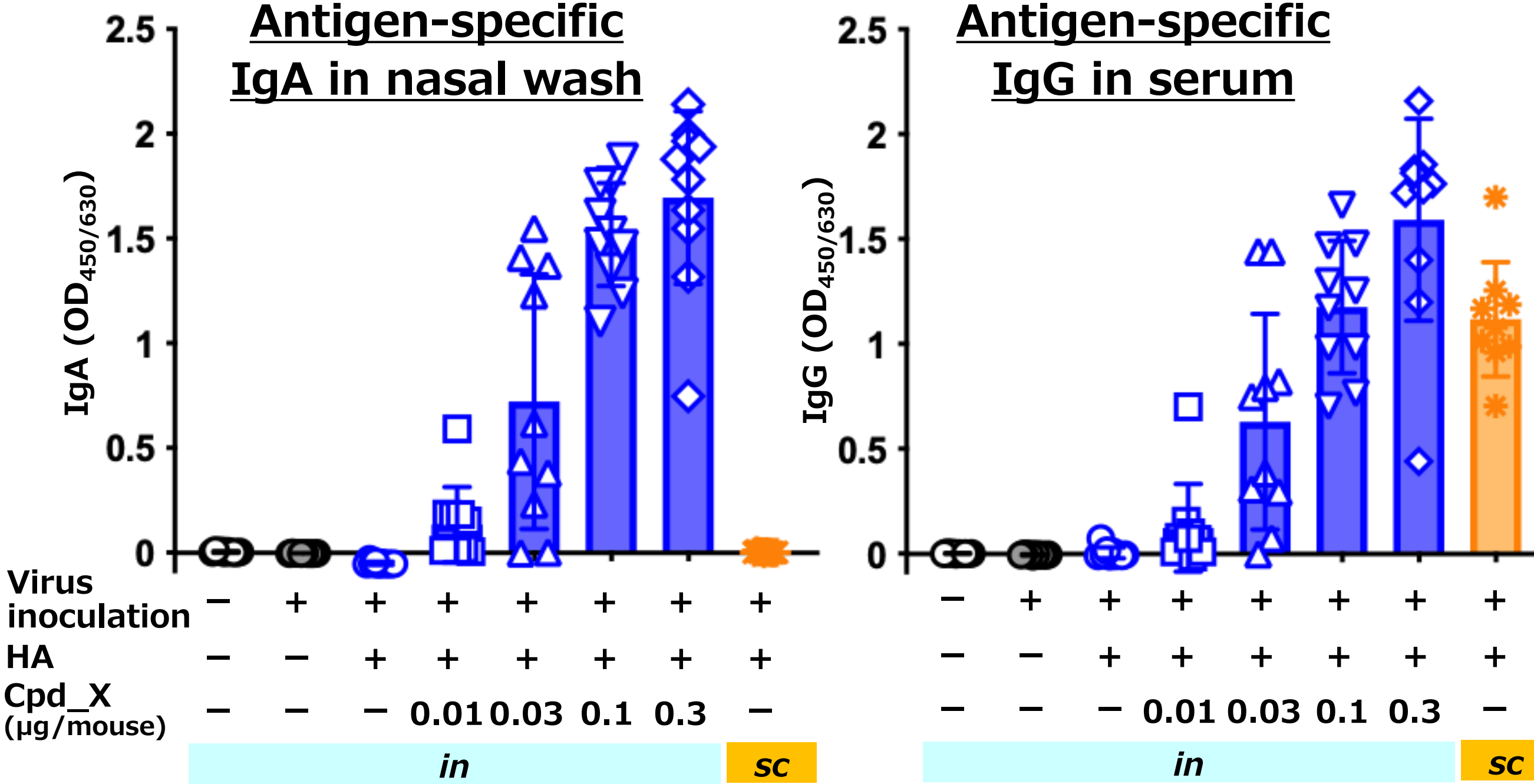
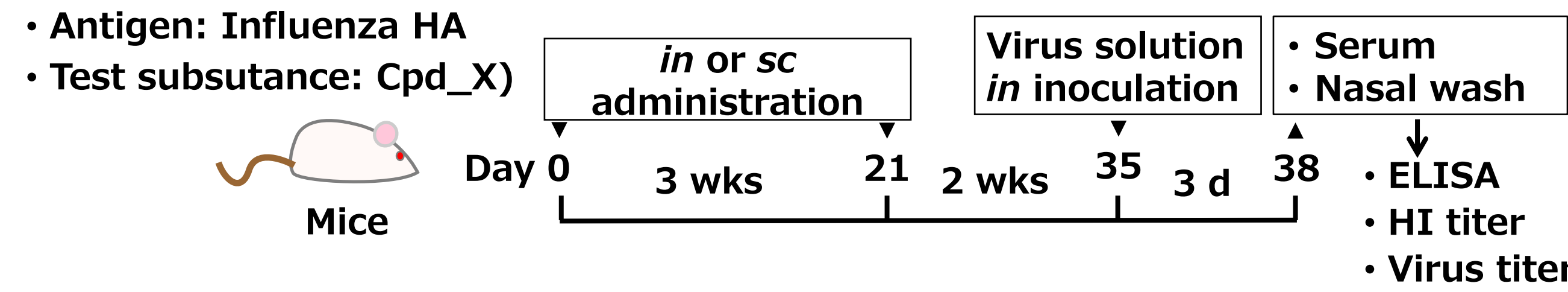


Nasal vaccines



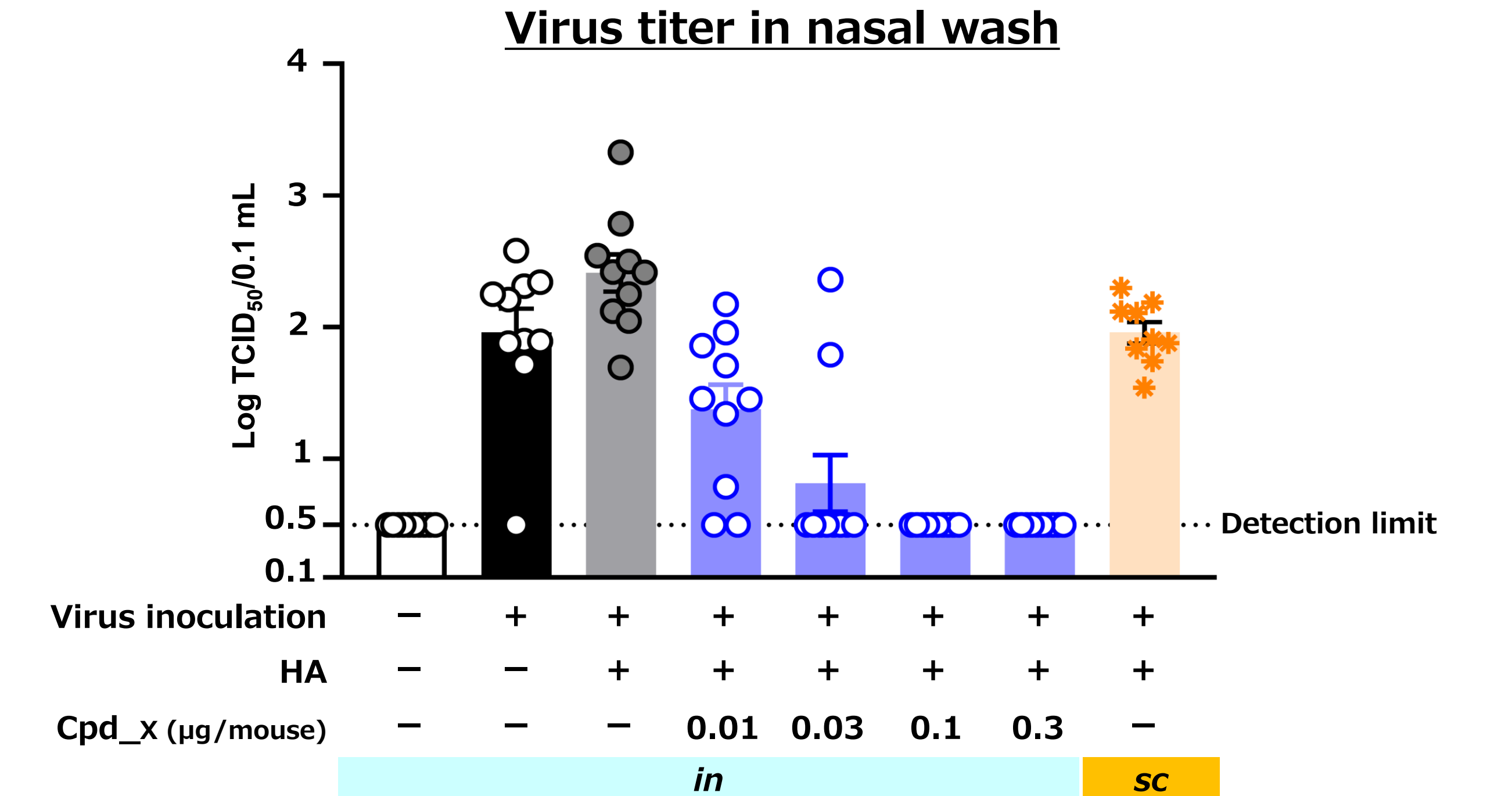
Target of vaccines:	General infections	Respiratory tract infections (influenza, etc.)
Antibody induction site:	Blood (systemic)	Airway mucosa (local) Blood (systemic)
Antibody cross-reactivity:	Low	High
Antibody type:	Blood: IgG	Mucosa: Dimeric IgA Blood: IgG
Expected effects:	Prevention: Onset, Aggravation	+Infection preventive effect Prevention: Onset, Aggravation

Intranasal administration of HA+Cpd_X induced IgA in the nasal mucosa and IgG in blood, and protected against viral infection



Serum HI titer	Virus inoculation	-	+	+	+	+	+	+
	HA (µg)	-	-	0.1	0.1	0.1	0.1	0.1
	Cpd_X (µg)	-	-	-	0.01	0.03	0.1	0.3
	Route	-	-	in				sc
Geometric mean Ab titer (GMT)		5.0	5.0	5.0	6.6	17.4	40.0	69.6
GMT change rate (>2.5)		-	1.0	1.0	1.3	3.5	8.0	13.9
Seroconversion rate (≥titer; 1:40, GMT change rate≥4)		-	0/10	0/10	1/10	4/10	7/10	9/10
		-	0%	0%	10%	40%	70%	90%

() : EMA criteria for evaluating the effectiveness of influenza vaccines



Development Process & Data Package



3 candidate compounds

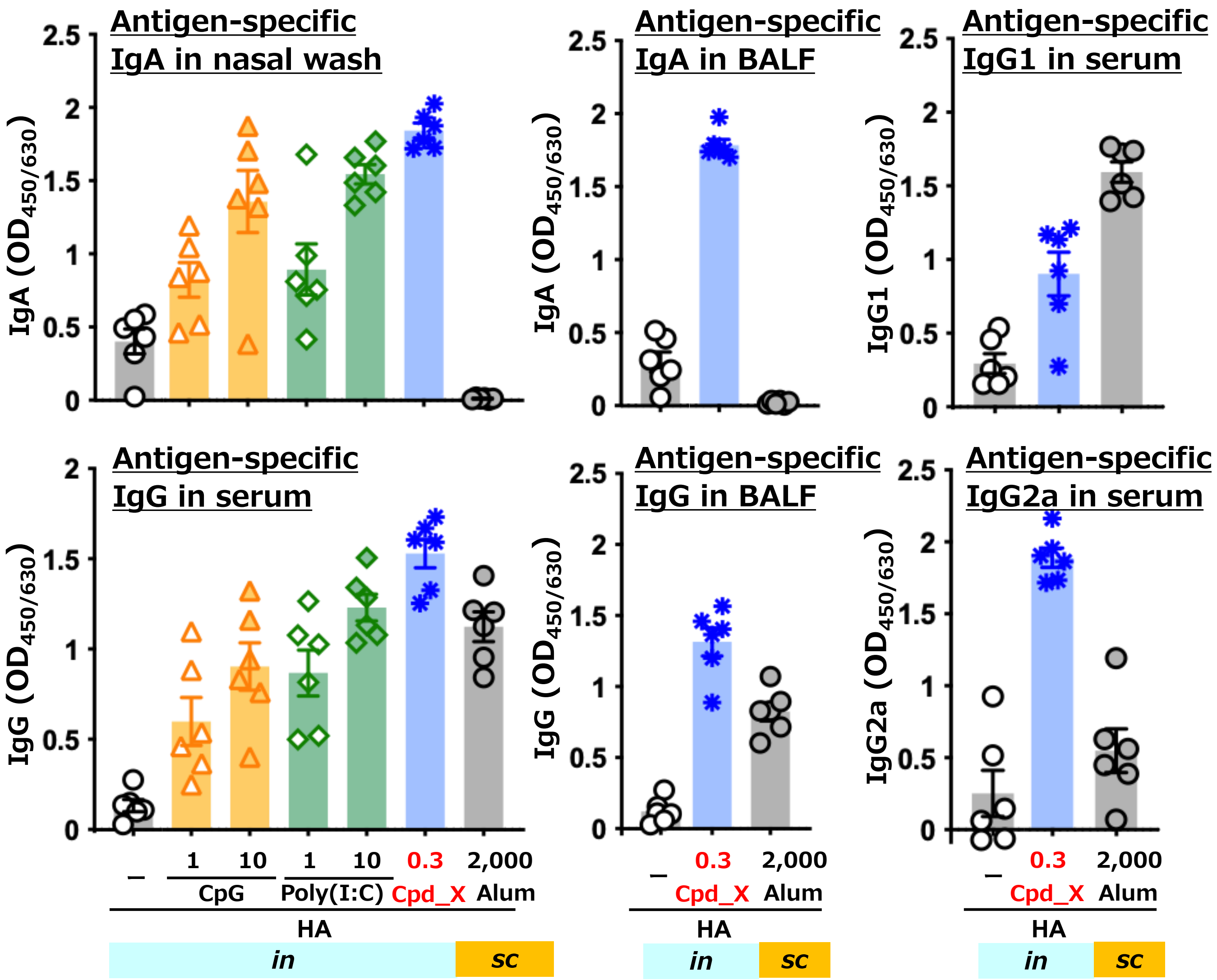
Studies for practical application
1. Safety
2. Pharmaceuticals
3. Synthesis methods

Novel mucosal adjuvant
Compound X (Cpd_X)
(Dual TLR agonist structures)

Data package (under CDA)

[Substance information] ·Synthesis method, Purity, Physicochemical properties ·Stability [Safety studies] ·Non-GLP preliminary studies> ·Single-dose preliminary study (mice, rats) ·In vitro genotoxicity preliminary study [Efficacy] ·Adjuvant activity in mice administered intranasally (mice, rats). ·Influenza vaccine HA antigen (Split)	[Intellectual property information] ·Patent application files for Cpd_X [Pharmacokinetics, etc] ·Non-GLP preliminary study ·Plasma concentration measurement method ·Stability test for compound in plasma ·SARS-CoV-2 Spike protein antigen (Recombinant)
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Cpd_X induced antibody production at lower doses compared to CpG ODN (TLR9 agonist) and Poly(I:C) (TLR3 agonist)



Summary

- Intranasal administration of Cpd_X with influenza HA antigen:
 - 1) induces antigen-specific IgA antibody in nasal mucosa and IgG antibody in serum, and enhances serum HI titer.
 - 2) exhibits the protective ability against influenza virus infection that is not seen with the HA subcutaneous vaccine.
- It was confirmed that IgA antibodies were induced not only in the nasal mucosa—the administration site—but also in bronchoalveolar lavage fluid.
- A comparison of serum IgG1 and IgG2a levels revealed that Cpd_X acted to promote a Th1-dominant response.
- Cpd_X induced antibody production at lower doses compared to CpG ODN (TLR9 agonist) and Poly(I:C) (TLR3 agonist).

Nasal vaccine using the mucosal adjuvant “Cpd_X” shows superior vaccine efficacy compared to subcutaneous vaccine (conventional type).

Cpd_X is a synthetic organic compound with TLR dual agonist structure. It is expected to be effective not only for split and subunit vaccines, but also for mRNA vaccines, etc. It is believed that it may become a useful mucosal adjuvant for nasal vaccines, etc.

We are ready to provide Compound X under MTA

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