European NOVADUCK
(vector vaccines for ducks)
and
LyonBioPole GAP
(grippe aviaire pandémique)
research projects

Michel Bublot, Merial R&D

Montpellier, December 15, 2008

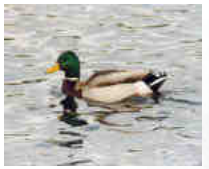
European Project NOVADUCK

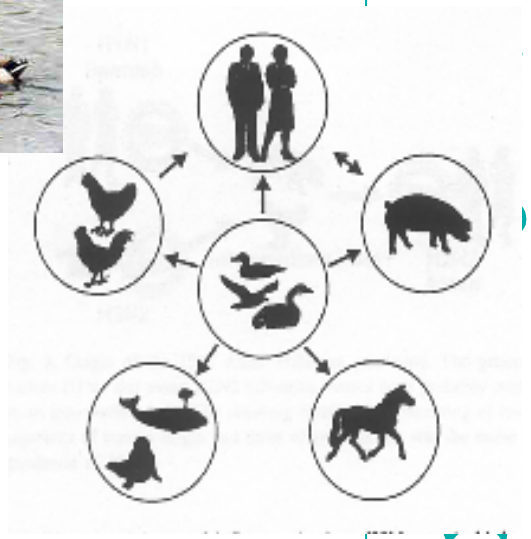
www.novaduck.eu

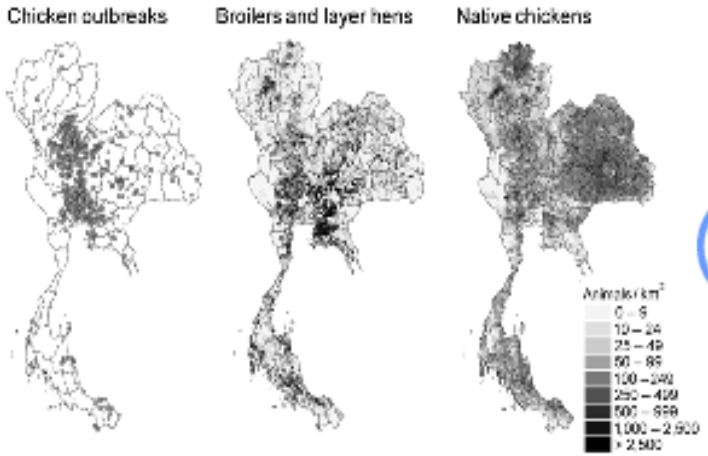
Novel recombinant DIVA vaccines for ducks

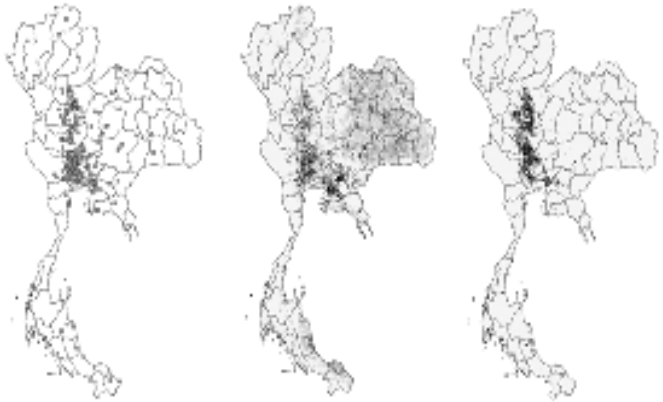
Why ducks ?

- Waterfowls: reservoir of influenza A
- Grazing ducks
- Important epidemiological role









NOVADUCK Partners

January 2007

COORDINATOR

MERIAL

afssa
AGENCE FRANÇAISE DE SÉCURITÉ SANITAIRE DES ALIMENTS
FRENCH FOOD SAFETY AGENCY

VAR

VMRI

CVI

Veterinary Laboratories Agency

BIOSOURCE
Epixis

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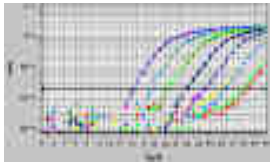
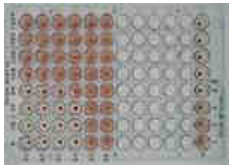
NOVADUCK WORKPACKAGES (1)

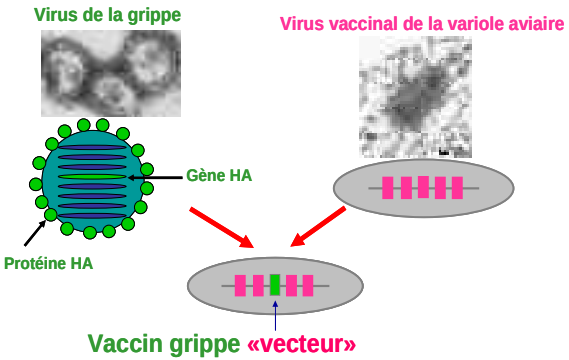




– WP1 – Preparatory phase

– WP2 – Vector vaccine generation:

- Selection of optimal AI gene:
  - HA
  - VLP retrovirus



- Development of 3 viral vectors

– WP3 – Immune response analysis:

- Humoral, cellular, mucosal
- DIVA test

NOVADUCK WORKPACKAGES (2)

CVI

- WP4 - Immunogenicity in ducks
  - Compare immune response
  - Check safety

afssa

Veterinary Laboratories Agency

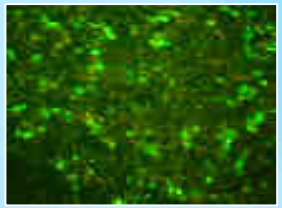
- WP5 – Efficacy in ducks
  - Challenge model set up
  - Compare protective response
  - Evaluate potential drift

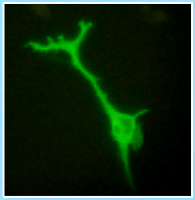
NOVADUCK : Novel Avian Influenza DIVA recombinant vaccines for ducks.

WP02 : Comparaison de l'immunogénicité de différents gènes de l'hémagglutinine de sous-type H5 d'influenzavirus aviaire en utilisant la vaccination ADN chez le canard de barbarie

- Gènes clonés dans un vecteur d'expression

- Expression protéique vérifiée en Immunofluorescence





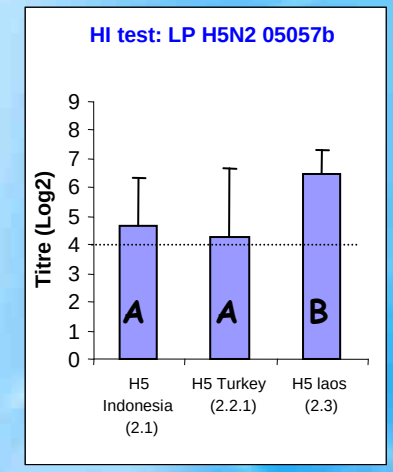
- **Animaux** : Canards de barbarie EOPS (AFSSA Ploufragan) âgés de 5 semaines (15/groupe)
- **Protocole :**

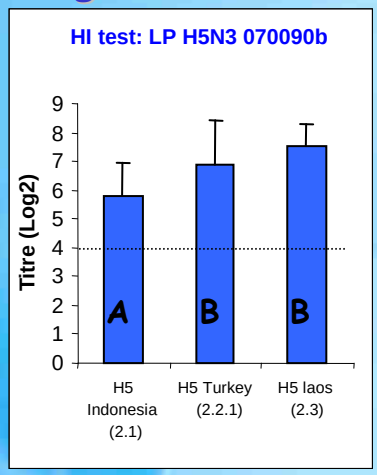
Eclosion — 1ère prise de sang — 1ère injection ADN (5 semaines) — 2nde PS — 2nde injection ADN (8 semaines) — Saignement (11 semaines)

- **Evaluation de l'immunogénicité** : Tests sérologiques (IHA et SN)

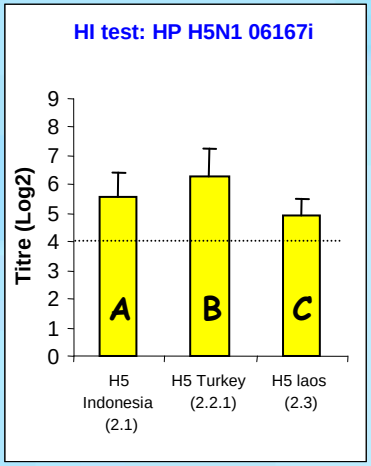
Comparaison des gènes H5 'optimisés'

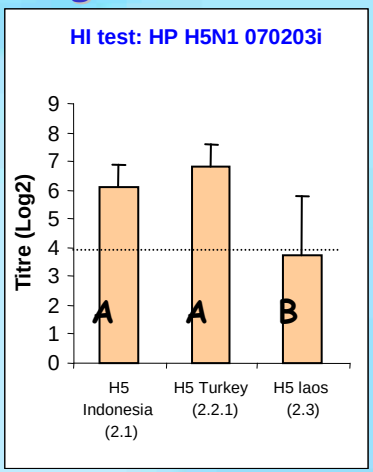
IHA avec Ag LP



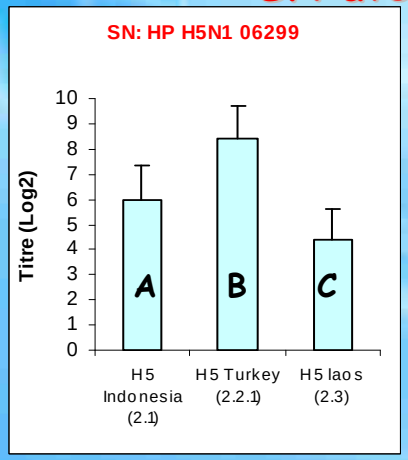


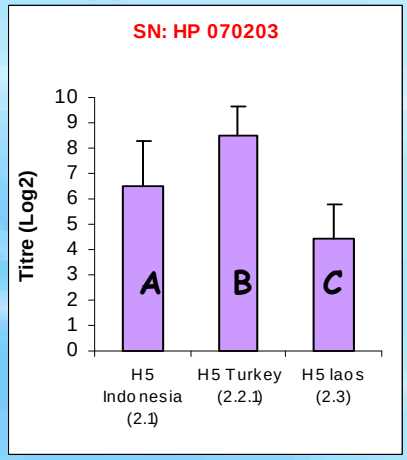
IHA avec Ag HP





SN avec virus HP

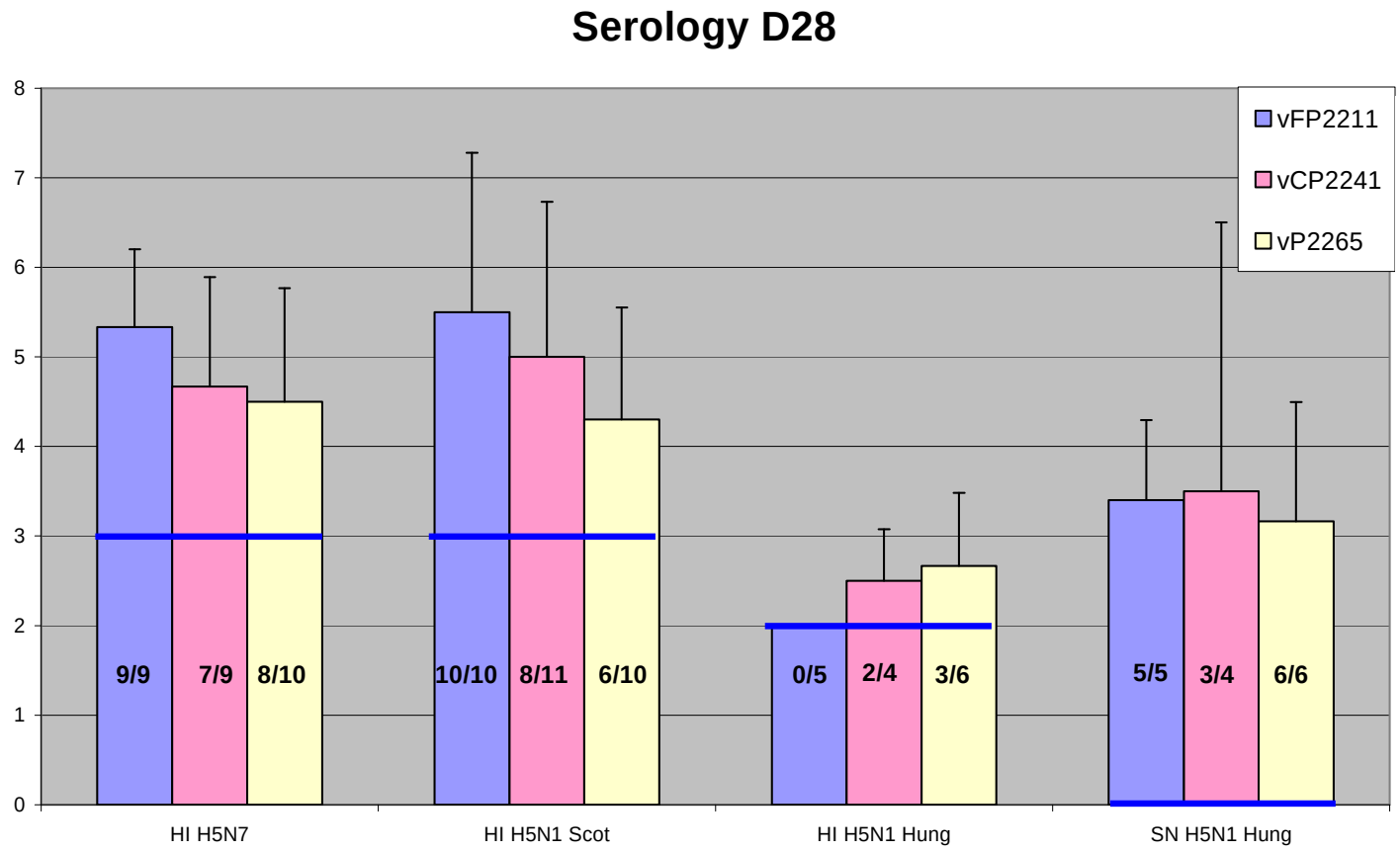




Conclusions : **LPAI : H5 Turkey and Laos : immunogénicité supérieure ou égale à H5 Indonesia**

HPAI : H5 Turkey : plus forte immunogénicité envers clades 2.2.1 and 2.2.3

Evaluation of 3 poxvirus vectors in ducks



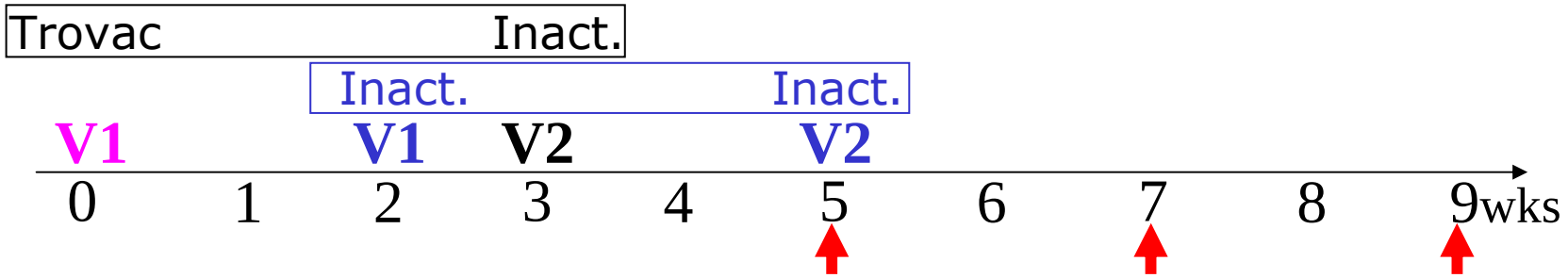
Fowlpox (TROVAC)
Canarypox (ALVAC)
Vaccinia (NYVAC)

Day-old Muscovy

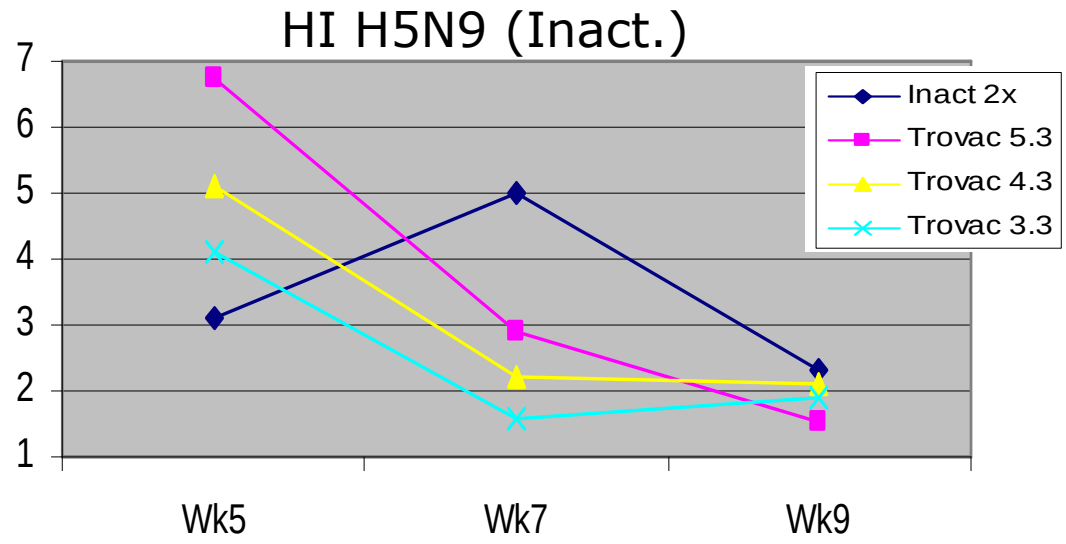
D0: V1 5 log10
D21: V2 5 log10

Similar immunogenicity of the 3 vectors

Prime-boost in day-old Pekin ducks



Blood sampling



- Dose effect of Fowlpox vector (TROVAC) priming
- Quick decrease of HI titers

GAP (Pandemic Avian Flu)

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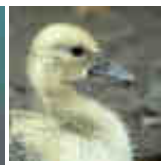


MERIAL

Vaccines

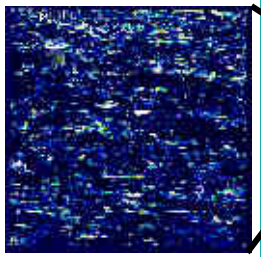
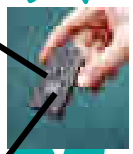
Diagnosis

sanofi pasteur
La division vaccins du Groupe sanofi-aventis.

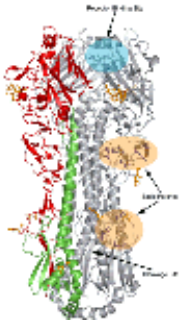
GAP

BIOMÉRIEUX

FONDATION MÉRIEUX

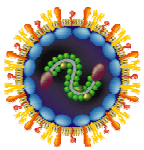



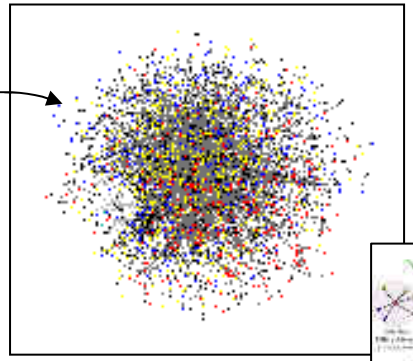
LABORATOIRE PL JEAN MÉRIEUX



Hôpitaux de Lyon

Inserm





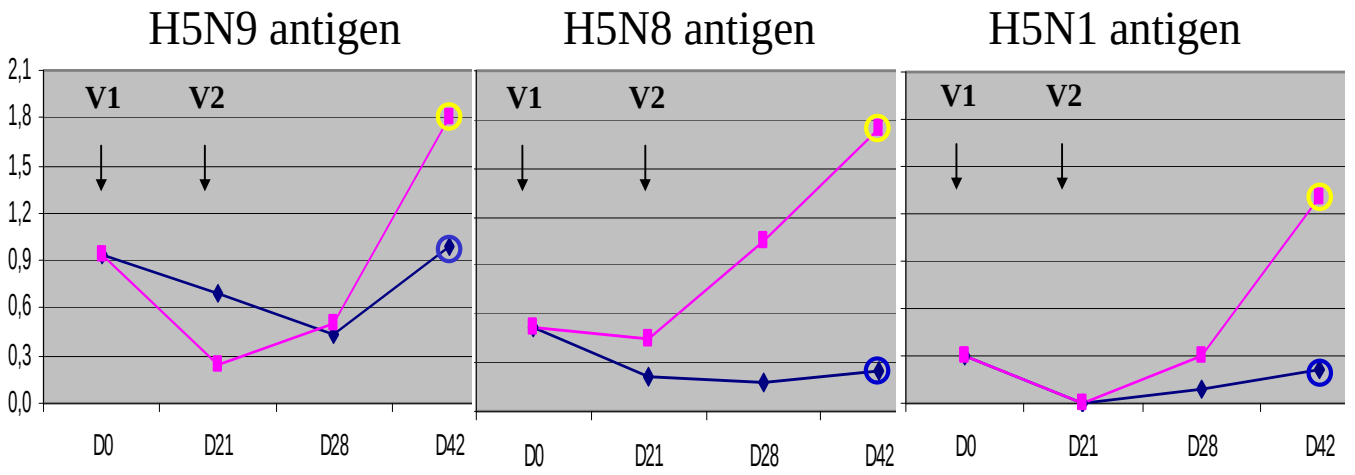

Interactome

«Heterologous prime-boost » scheme

- V1: Fowlpox-HA vector at day-old
- V2: Inactivated vaccine

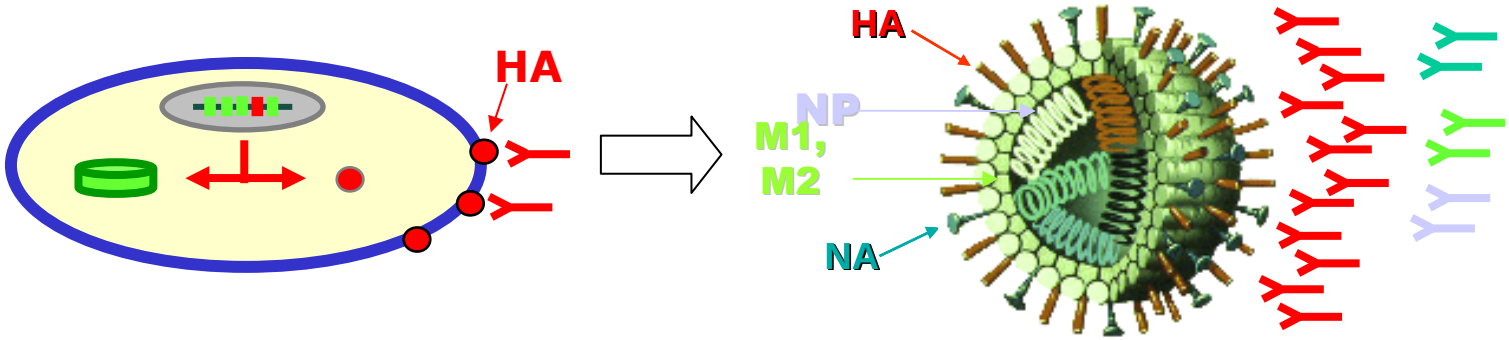
V1 à J0	V2 à J21
Inact. H5N9	Inact. H5N9
FP-HA (H5N8)	Inact. H5N9

Ac. Mat. +

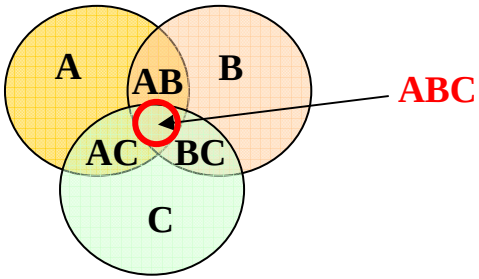


Prime-boost principle

1. **Different antigen presentation**
   - **Fowlpox**: Cell-Mediated Immunity
   - **Inactivated**: Humoral Immunity
2. **Boost directed to protective antigen** (HA)



3. **Boost with a different HA** to increase response against conserved epitopes (broader response)



B + B ⇒ B mainly	**(2 shots of inact.)**
AB +AB ⇒ A + B mainly	**(2 shots of biv. inact.)**
A + B ⇒ AB + ABC	**(prime-boost)**

Bublot *et al.* (2008) Res. Sign Post 37/661(2), 117-136

Prime-boost concept

- **Advantages**:
  - 1st vaccination at the hatchery ⇒ Early onset
  - Only 1 administration with adjuvant at the farm
  - Broader antibody response
  - Multispecies (chickens & ducks)
  - Lower risk of influenza drift ???
- **Future**:
  - Evaluate the boost with subunit HA protein (DIVA)

Conclusion

- Benefits of collaborative projects
- Promising prime-boost strategy

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