Genetic determinants for virulence and adaptation of clade 2.3.4.4 H5N8 viruses in ducks

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Junior scientist symposium November 2022

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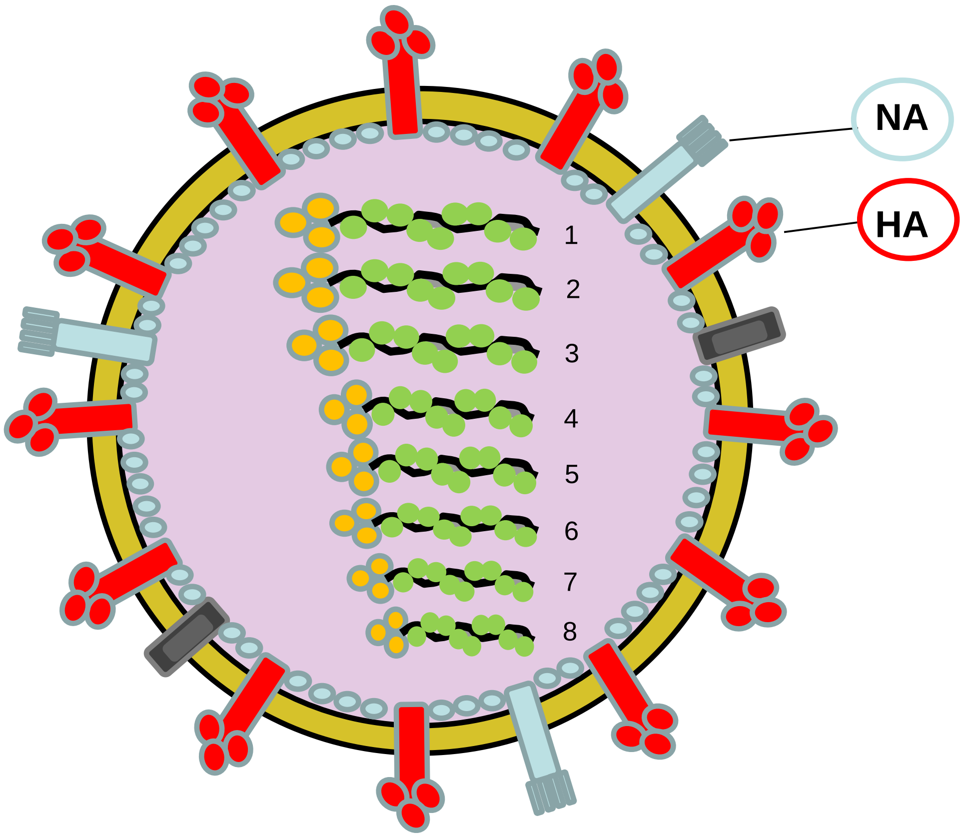
Introduction

Avian Influenza Virus
(classical fowl plague, bird flu)



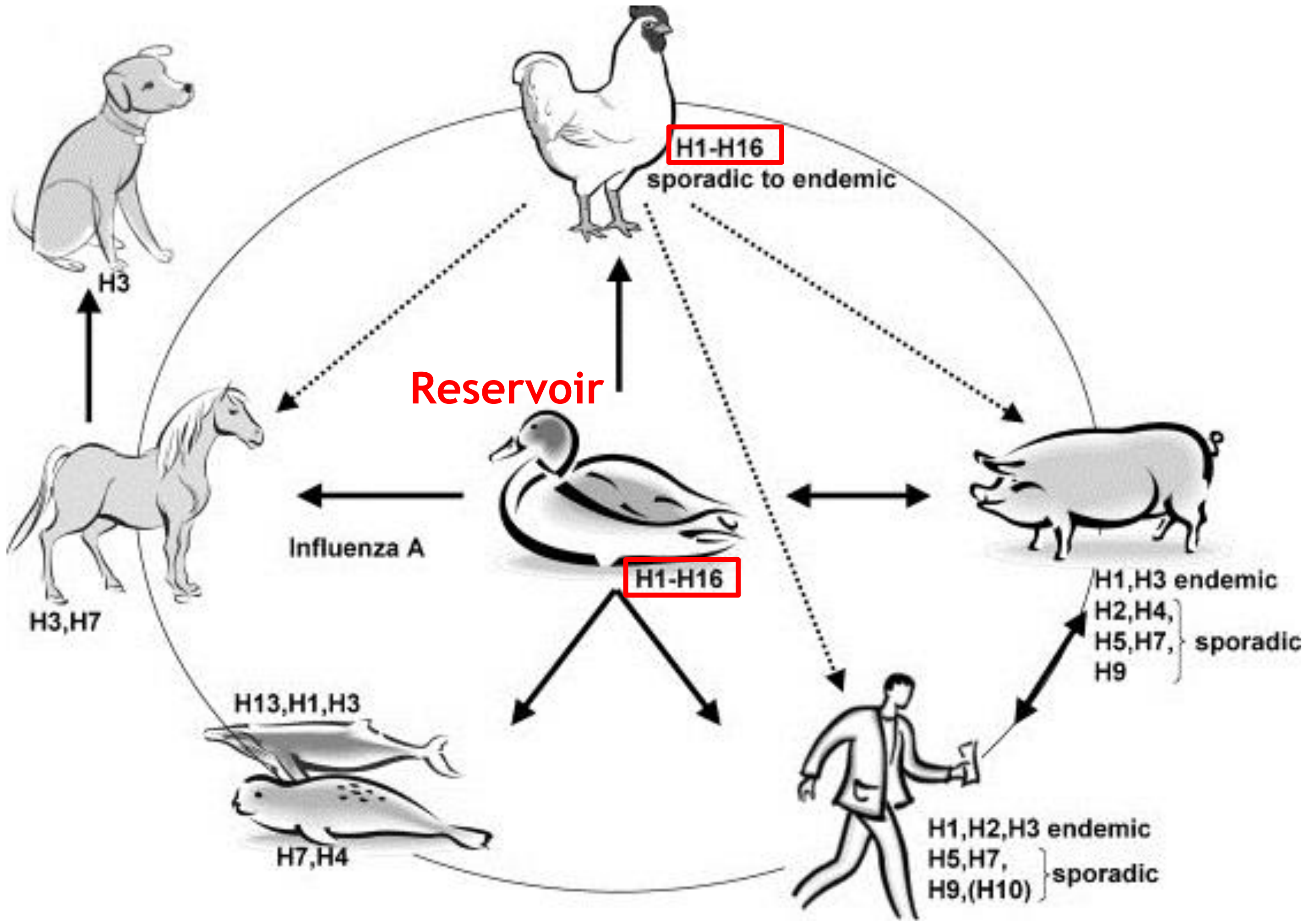
Family: *Orthomyxoviridae*
Genus: Influenza A virus

Genome: single stranded RNA,
negative polarity,
8 segments
at least 10 viral proteins
enveloped

Subtypes: Hemagglutinin (HA) 1-16
(Attachment, Fusion)
Neuraminidase (NA) 1-9
(Virus release)

16 x 9 = 144 subtypes in total

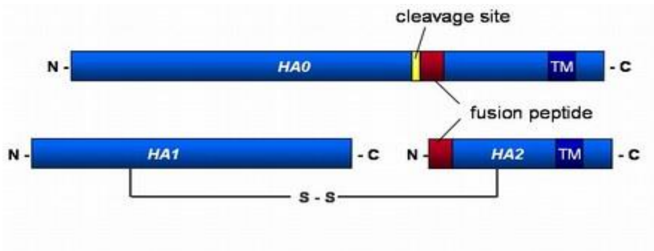
Introduction



(Kalthoff et al., 2010)

AIV pathotypes (particularly in galliformes)

Main virulence determinant = proteolytic cleavage site within the hemagglutinin



LPAIV: HA monobasic cleavage site
-> trypsin-like proteases

HPAIV: HA polybasic cleavage site
-> subtilisin-like proteases (ubiquitous)

Intravenous pathogenicity index

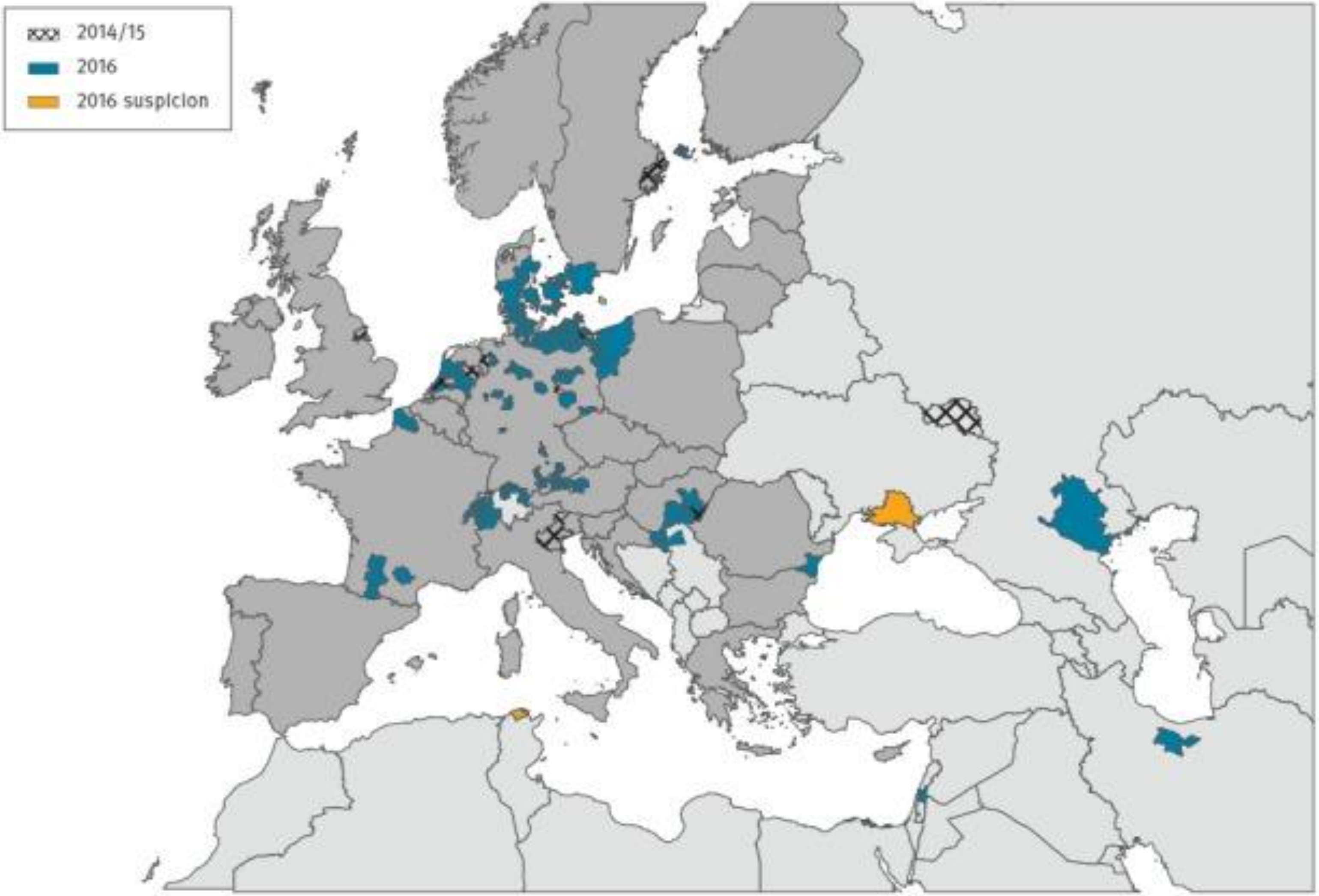
Clinical signs LP= 0 to 1.2

Respiratory disorders
Ruffled feathers
Low weight gain
Decrease in egg production

HP >1.2 to 3

Up to 100% mortality
Cyanosis
Dyspnea
Edema
Diarrhea
Neurological disorders

H5N8 2014 vs 2016



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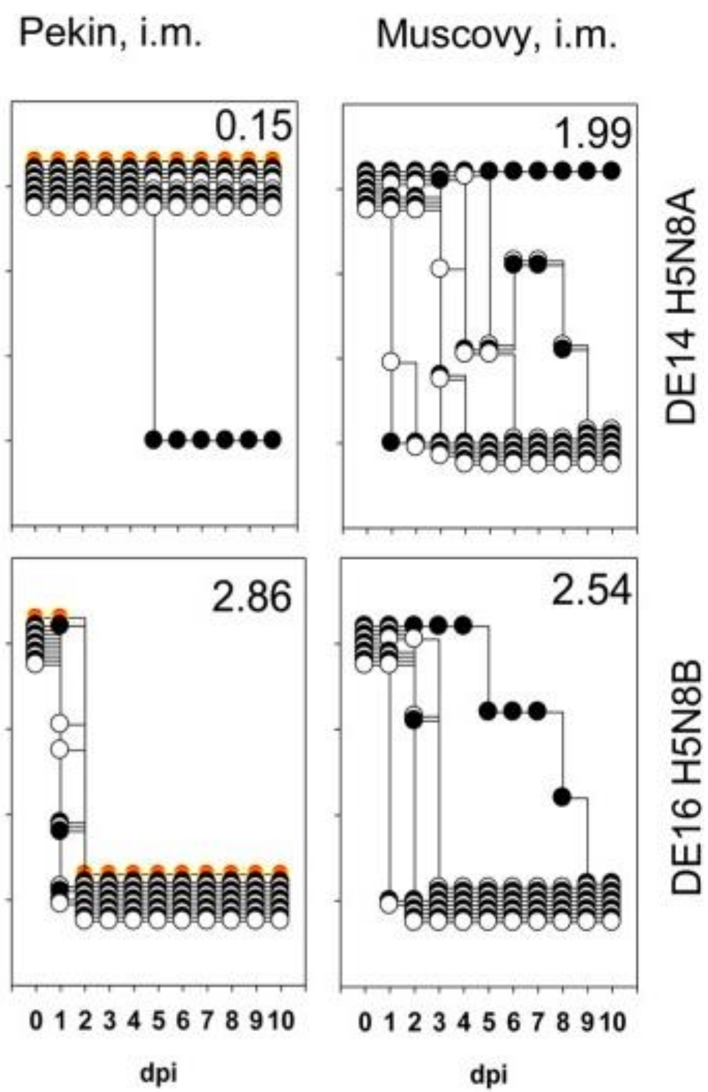
H5N8 14 vs 16 in ducks

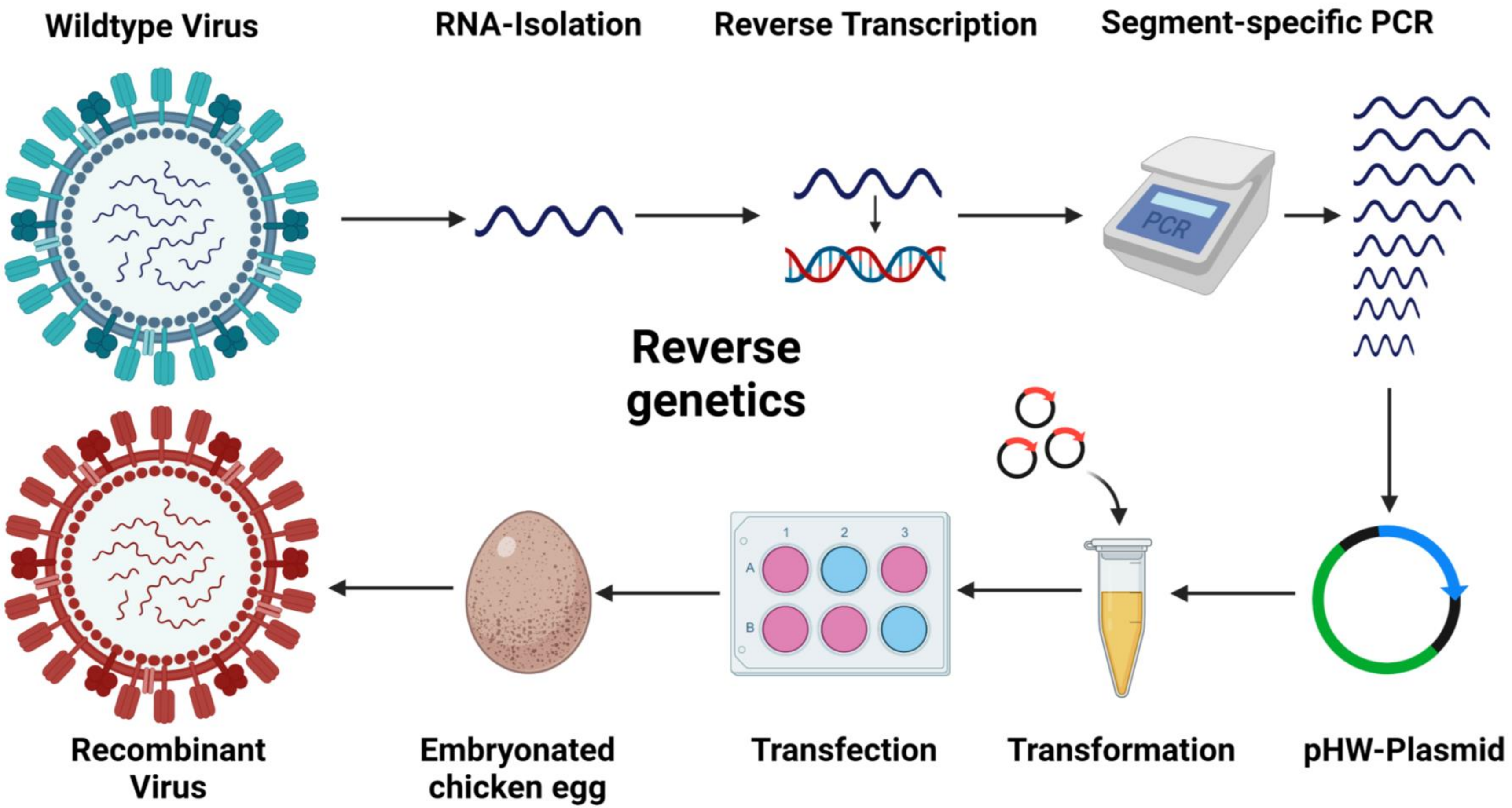


Higher susceptibility of Muscovy ducks

Higher virulence of H5N8 2016 in Pekin ducks

Grund et al. 2018

Generation of recombinant viruses



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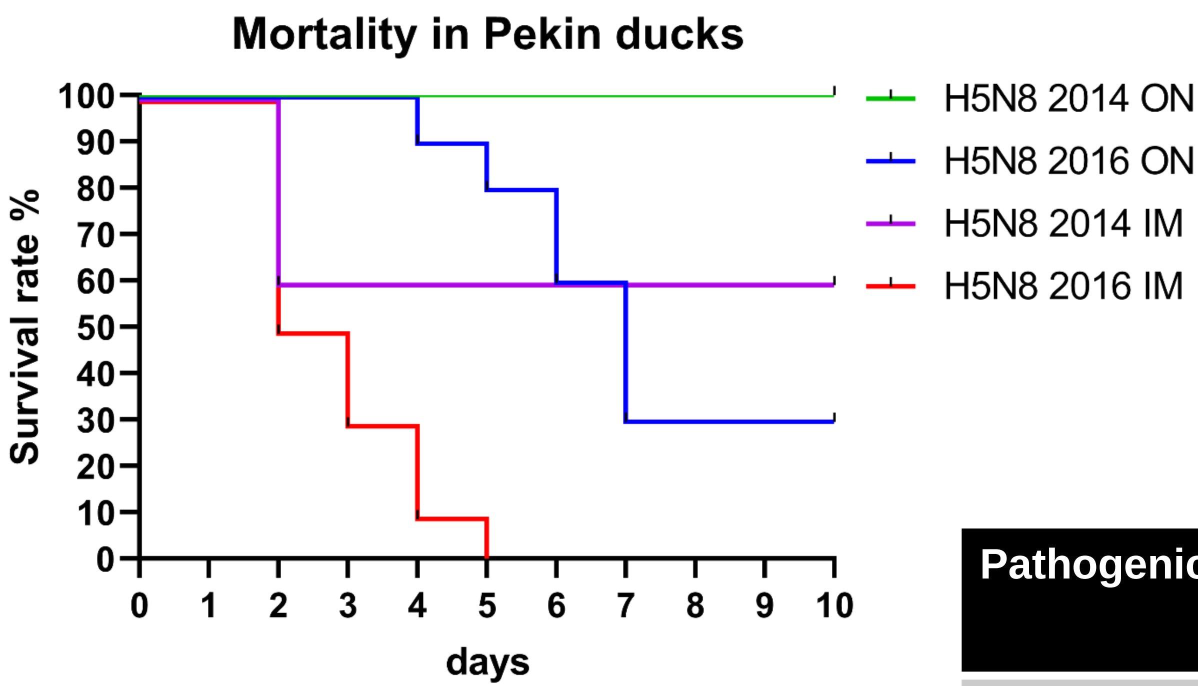
Confirmation of these results with recombinant viruses



Pathogenicity index	IM	ON
H5N8 2014	1.15	0
H5N8 2016	2.6	2.5

HA-Reassortants

Virus	Scoring	Mortality	MDT (days)	Mortality Contact Birds	Seroconversion
H5N8 2014	0	0/10	/	0/5	100%
H5N8 2014 +HA 16	0	0/10	/	0/5	100%
H5N8 2016 +HA 14	0	0/10	/	0/5	100%
H5N8 2016	2.5	10/10	3.1	5/5	/

Double-Reassortants

Virus	Scoring	Mortality	MDT (days)	Mortality Contact Birds	Seroconversion of Survivors
H5N8 2014 +HA, PB2 16	0.3	0/10	/	0/5	100%
H5N8 2014 +HA, PB1 16	0	0/10	/	0/5	100%
H5N8 2014 +HA, PA 16	0	0/10	/	0/5	100%
H5N8 2014 +HA, NP 16	0.6	1/10	8.5	2/5	100%
H5N8 2014 +HA, NA 16	0.3	1/10	4	1/5	100%
H5N8 2014 +HA, M 16	0.3	1/10	/	0/5	100%
H5N8 2014 +HA, NS 16	0.3	1/10	5	1/5	100%
H5N8 2016	2.4	10/10	3.9	5/5	/

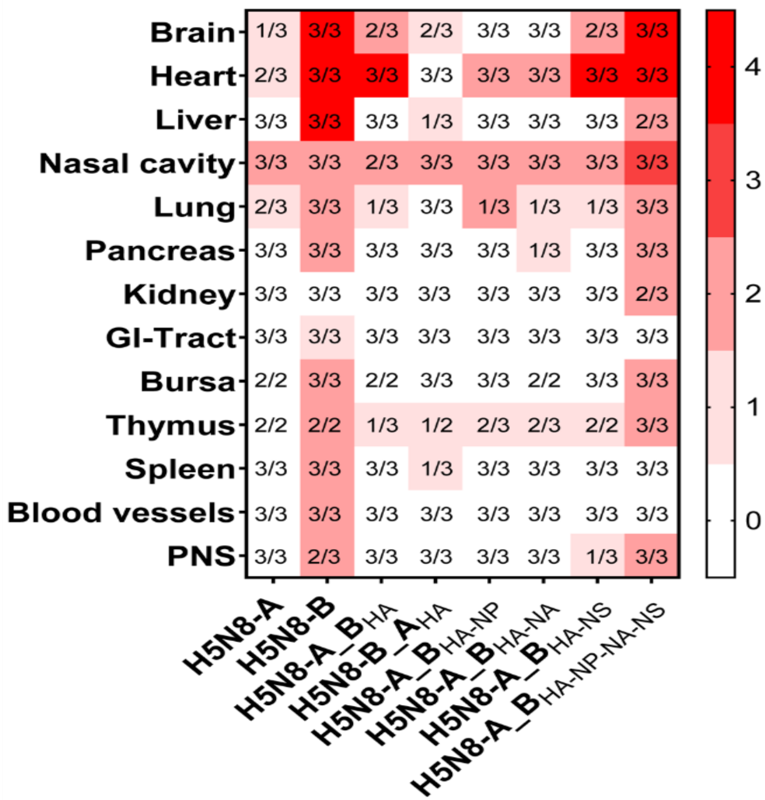
Multi-Reassortants

Virus	Scoring	Mortality	MDT	Mortality Contact Birds	Seroconversion of Survivors
H5N8 2014 +HA, P3 16	0	0/10	/	0/5	100%
H5N8 2014 +HA, NP, NA 16	1.4	3/7	5.3	3/5	100%
H5N8 +HA,					
H5N8 2014 +HA, NP, NA, NS 16	2.2	10/10	4.1	5/5	/
H5N8 2016	2.3	10/10	3.5	5/5	/

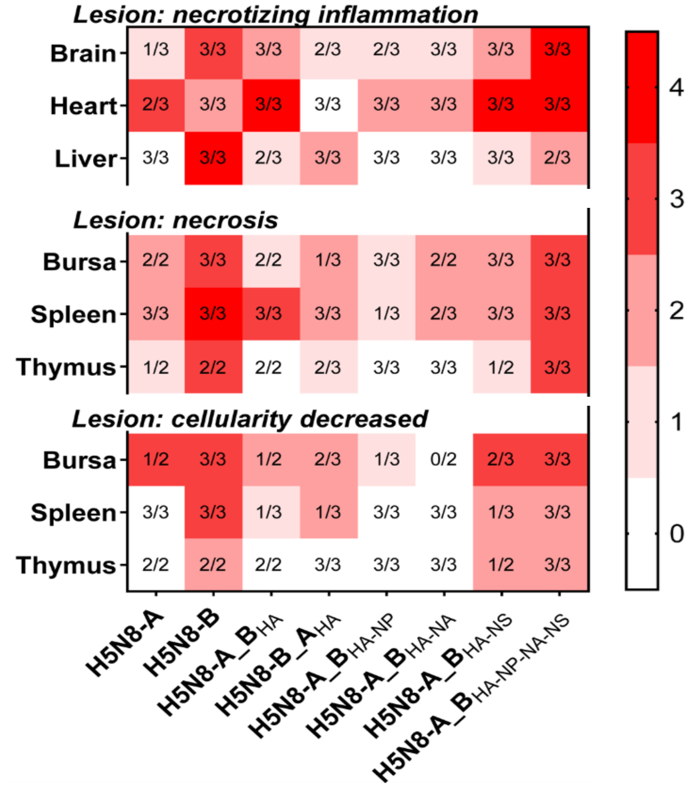
Minimal constellation for high virulence: HA, NP, NS

Pathology

Antigen Distribution

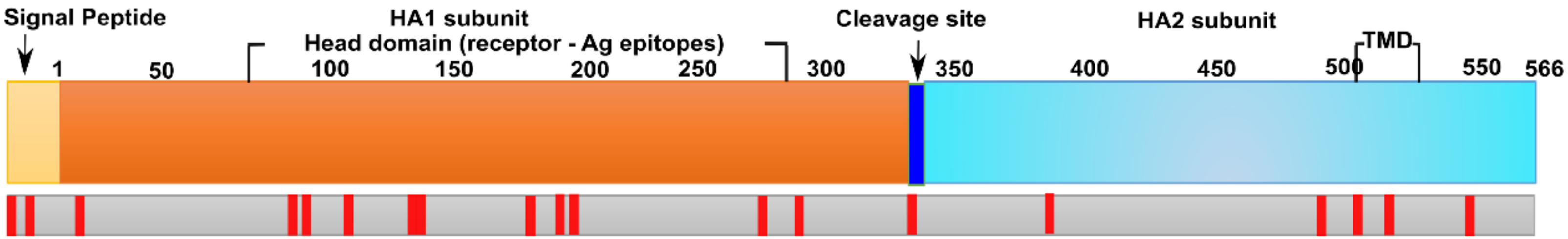


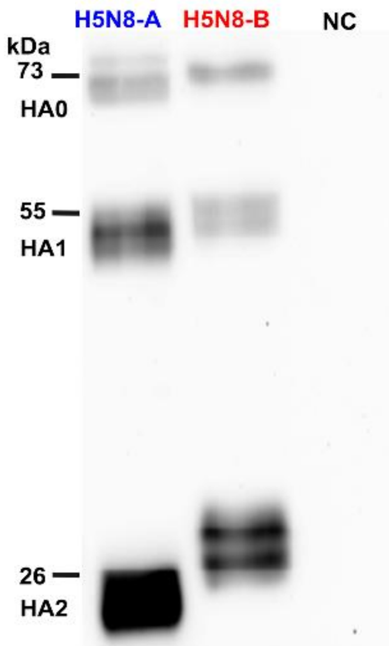
Histopathological changes

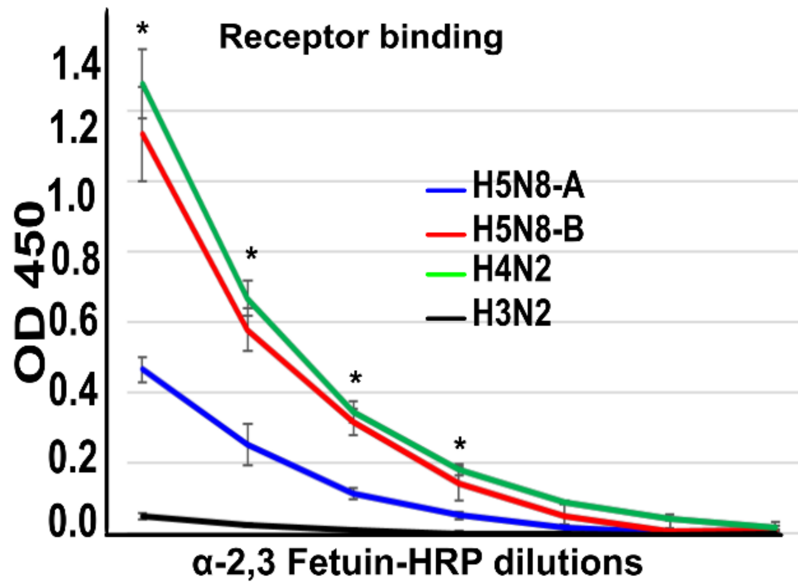


Hemagglutinin

H5N8-2014 *vs.* H5N8-2016: **<u>19 aa</u>**

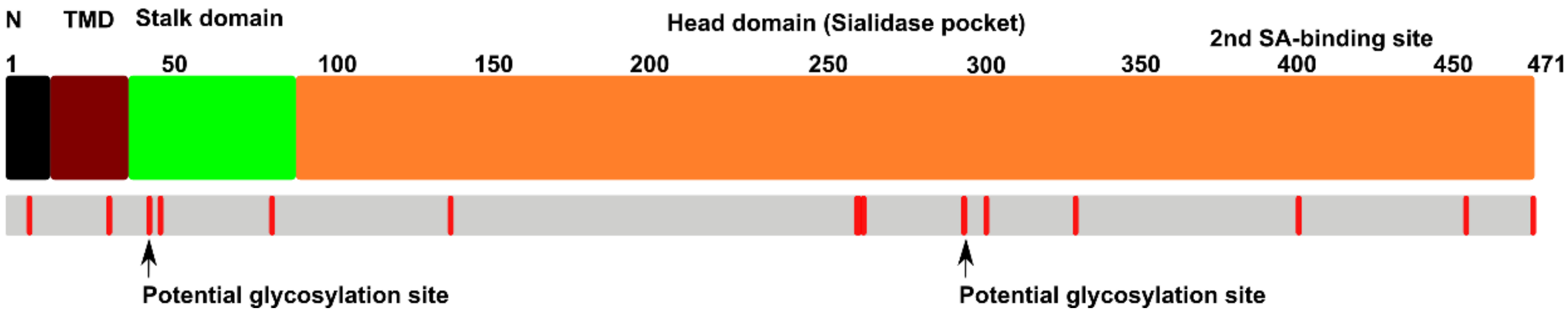


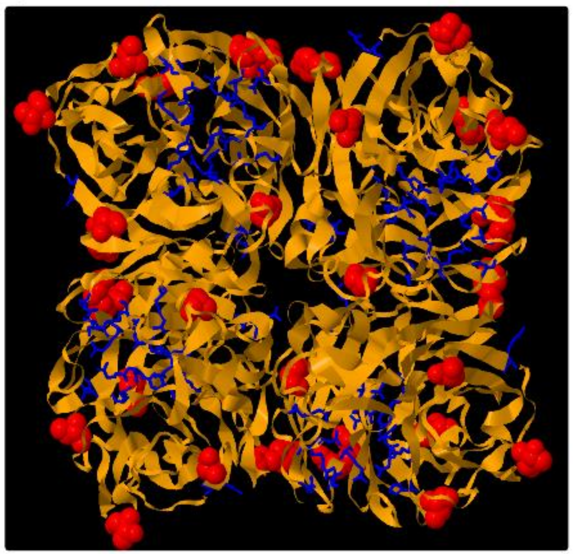


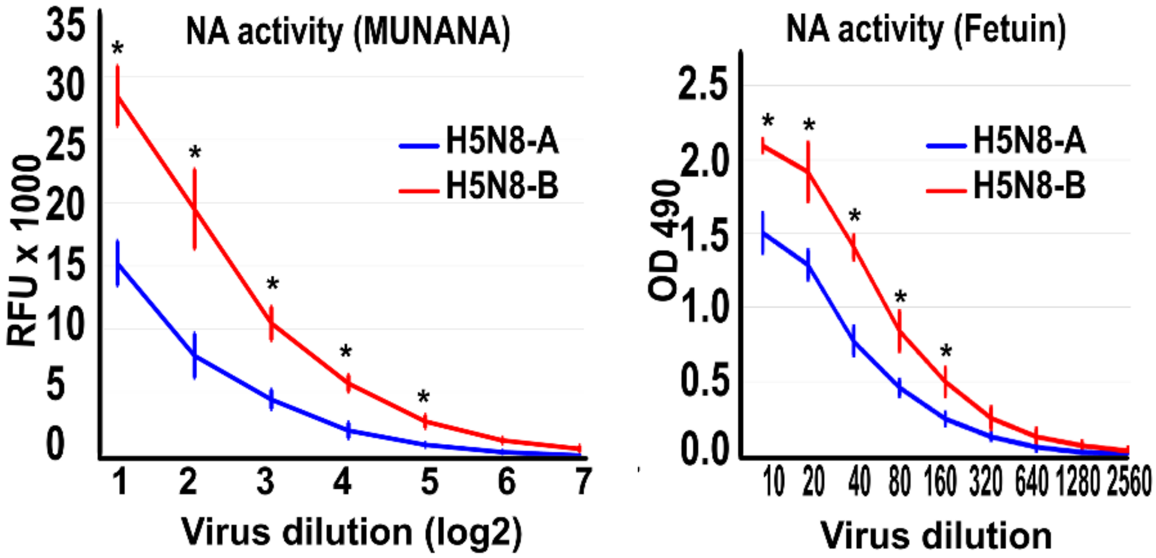


Neuraminidase

H5N8-2014 *vs.* H5N8-2016: **14 aa**

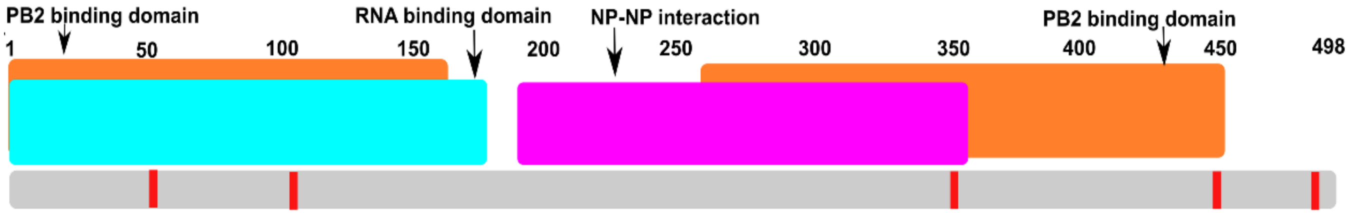


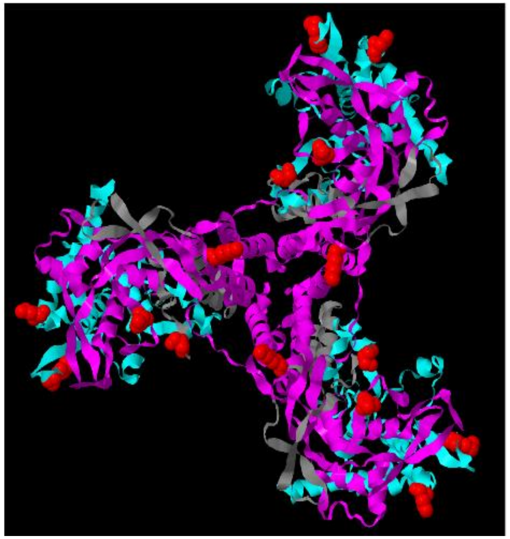


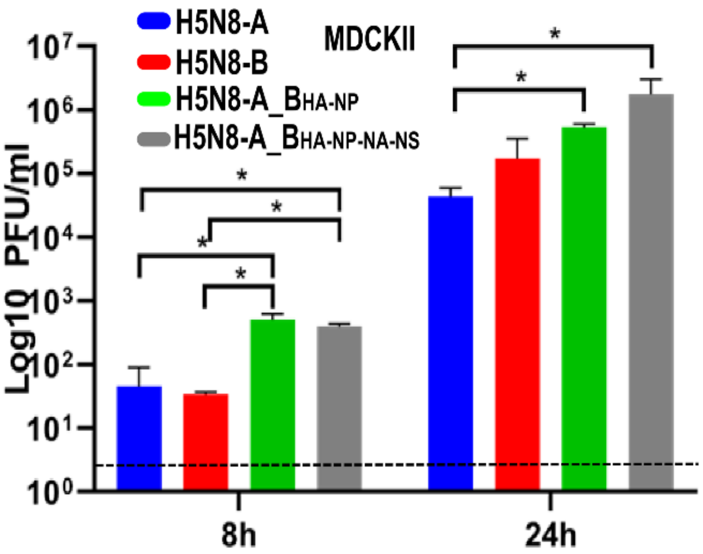


Nucleoprotein

H5N8-2014 *vs.* H5N8-2016: **NP 5 aa**

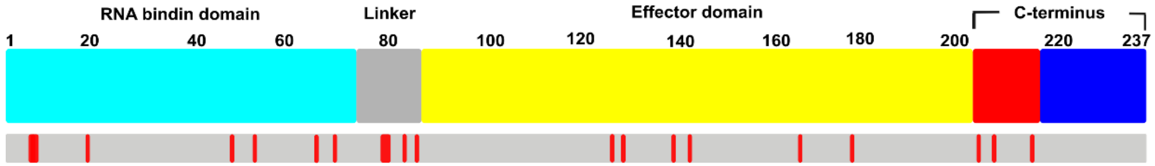


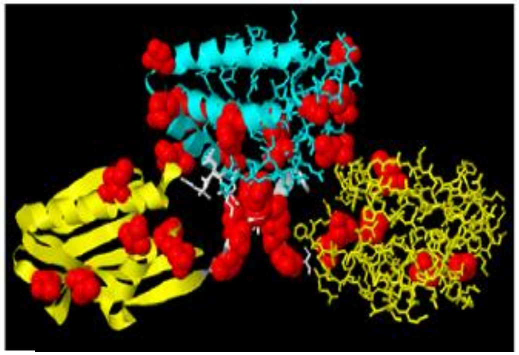


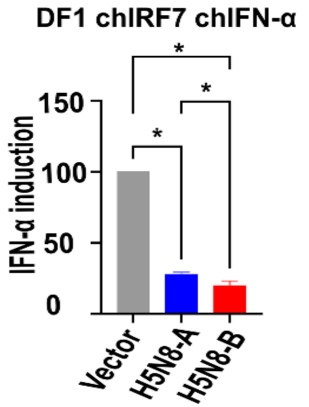


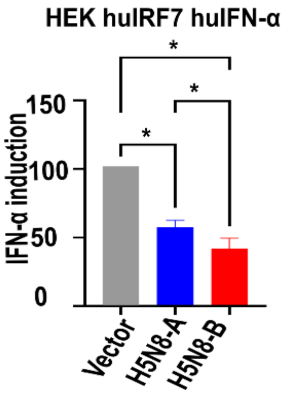
Non-structural protein 1

H5N8-2014 *vs.* H5N8-2016: **NS1 <u>20 aa</u>**

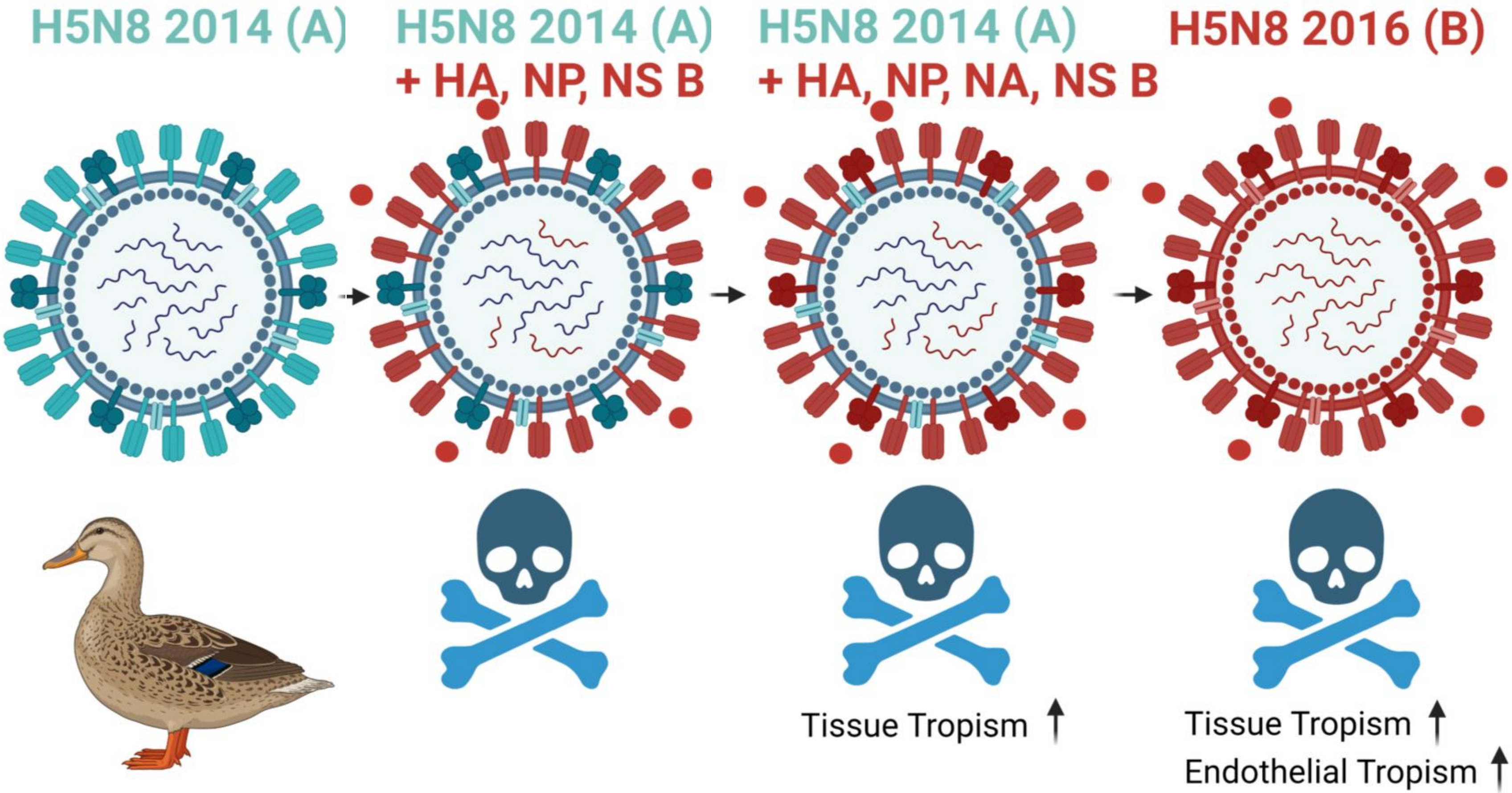








Conclusion



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Thanks to

El-Sayed M. Abdelwhab

Jutta Veits
Dajana Helke
Marcel Gischke
Claudia Blaurock
Maryna Kuryshko
Diana Palme

Angele Breithaupt
Silvia Schuparis

Timm Harder

Christine Luttermann

Thomas C. Mettenleiter

Stefan Finke

Thank you for your attention!

Charlotte Schröder
Bärbel Hammerschmidt
Animal caretakers

Christine Fast

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