

FluZooMark – a One Health Center

Viral and host factors of zoonotic and pandemic influenza A viruses

**Supported by Novo Nordisk Foundation:
Challenge grant 2019**

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Background – the burning platform

The average size of commercial swine herds has increased



Influenza in pigs is now an enzootic disease in swine herds



Significantly increased risk of re-assortment with human flu strains



Nowadays – more than 200 different influenza virus variants found globally

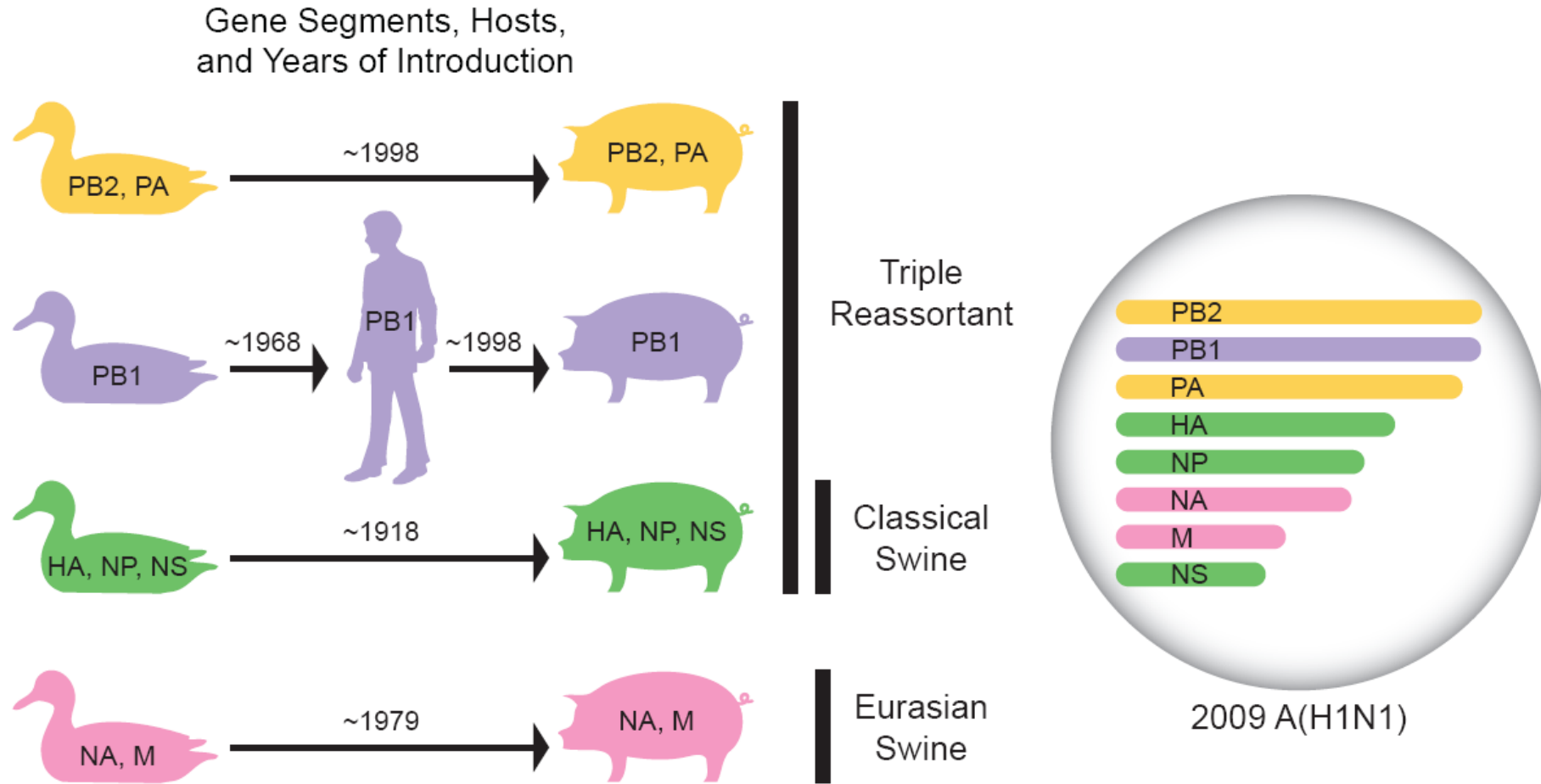


Many with zoonotic potential – one of them successful (2009 pandemic strain)



This may/will happen again!

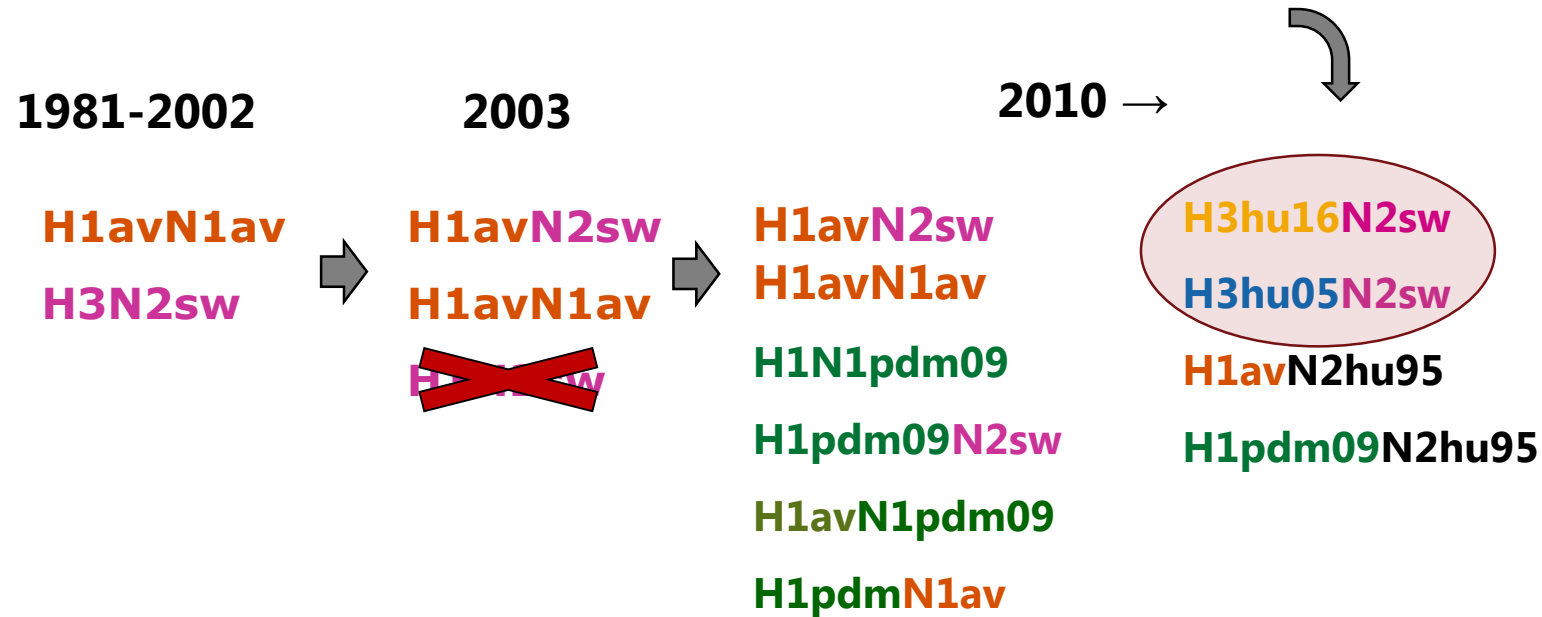
Pandemic 2009H1N1 - origin



Influenza A virus variants in pigs

Danish subtypes anno 2020:

Human seasonal influenza: **N2hu95**, **H3hu05**, **H3hu16**



In Denmark	21 different variants
In Germany	35 different variants
In China	> 100 different variants

Several reports on zoonotic transmission

Accepted: 14 February 2017
DOI: 10.1111/irv.12451

SHORT ARTICLE

WILEY

Triple-reassortant influenza A virus with H3 of human seasonal origin, NA of swine origin, and internal A(H1N1) pandemic 2009 genes is established in Danish pigs

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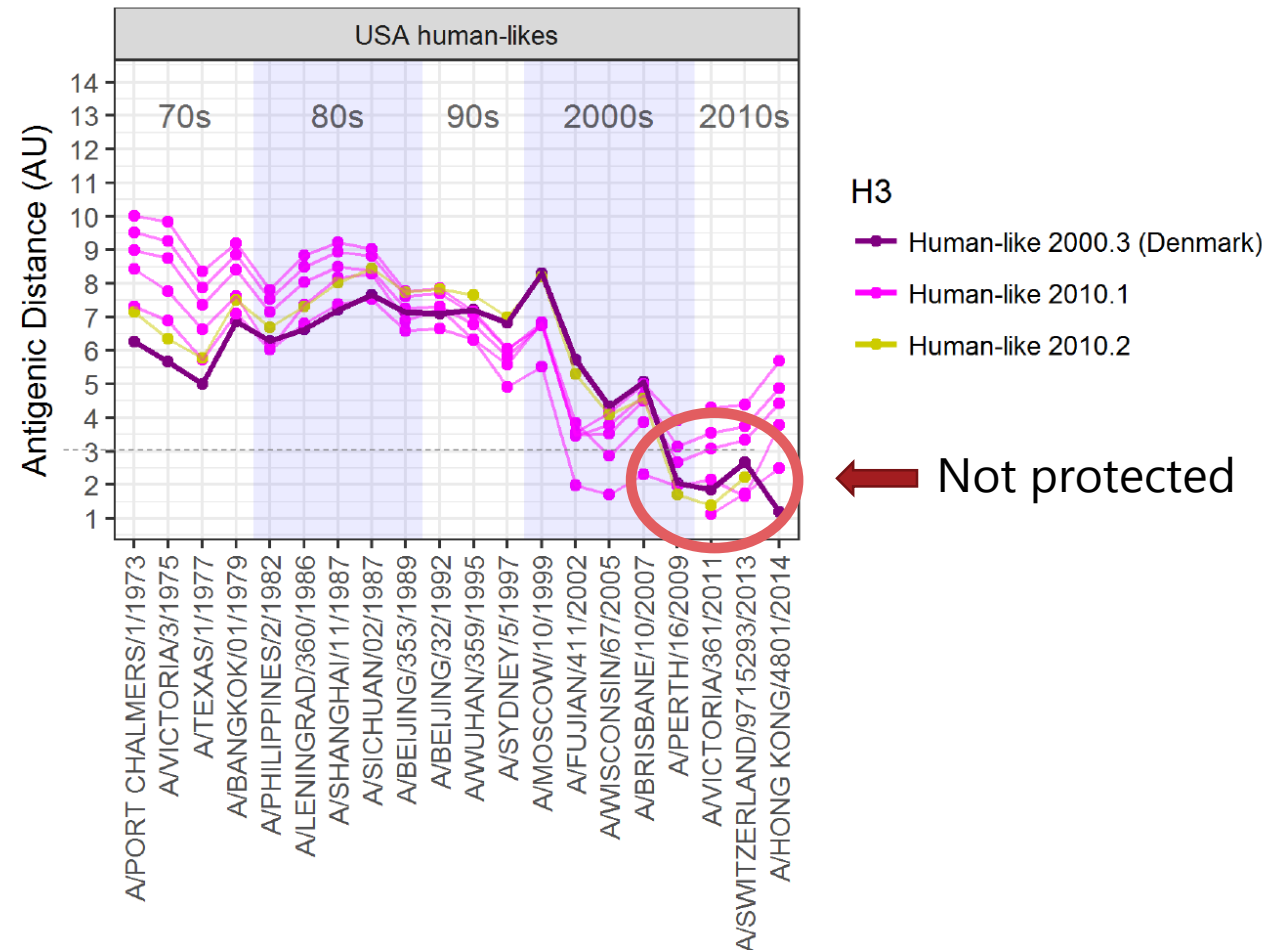
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This report describes a triple-reassortant influenza A virus with a HA that resembles H3 of human seasonal influenza from 2004 to 2005, N2 from influenza A virus already established in swine, and the internal gene cassette from A(H1N1)pdm09 has spread in Danish pig herds. The virus has been detected in several Danish pig herds during the last 2-3 years and may possess a challenge for human as well as animal health.

KEYWORDS
case report, H1N1pdm09, H3N2, influenza A virus, zoonosis

Antigenic Distance of Strains by H3 clade



State of the art – zoonotic potential of swIAV

- Increased swIAV surveillance globally since 2009
- Sustained number of sequences available in databases – no epidemiological data
- Very little information on swine innate immune responses to huIAVs and swIAVs
- Almost a complete lack of knowledge on host and viral markers for sustained infection of swine
- Profound lack of data on human innate immune responses to different swIAV

State of the art – IRAT – developed by CDC

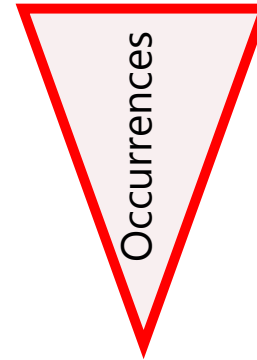
- Human infections
- Transmission in lab animals
- Receptor binding
- Existing population immunity
- Infection in animal species
- Genomic variability
- Antigenic relationship to vaccine candidates
- Global distribution (animals)
- Disease severity and pathogenesis
- Antiviral treatment susceptibility/resistance

Useful evaluation tool – NOT a tool for prediction

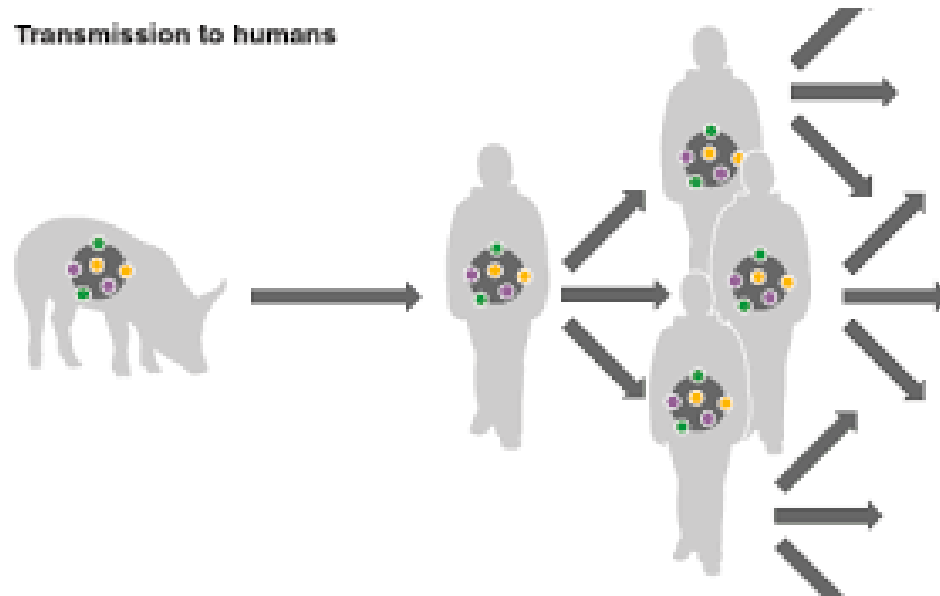
The Research Question – What?

Stages in pandemic development

- Stage 1. Strain widespread in swine
- Stage 2. One or few humans exposed
- Stage 3. Replication in humans
- Stage 4. Transmission locally
- Stage 5. Global spread



Transmission to humans

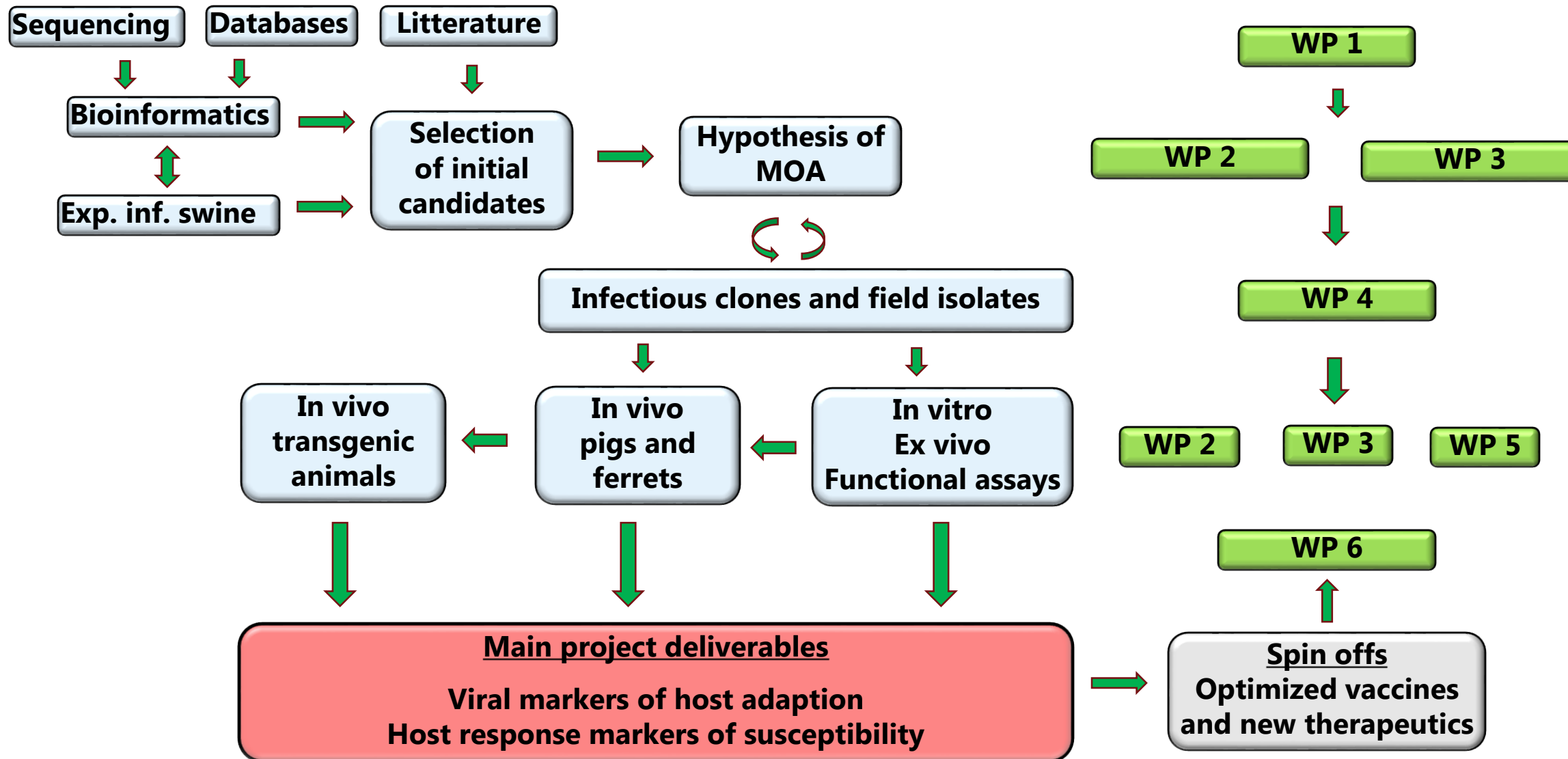


Aims of the project

Identify viral and host factors that increase the chance of a strain to progress beyond stage 2.

NB! nCorona virus (Wuhan) is these days moving from stage 4 to stage 5!

The Research Plan



The interdisciplinary One Health Consortium

Experts swine immunology



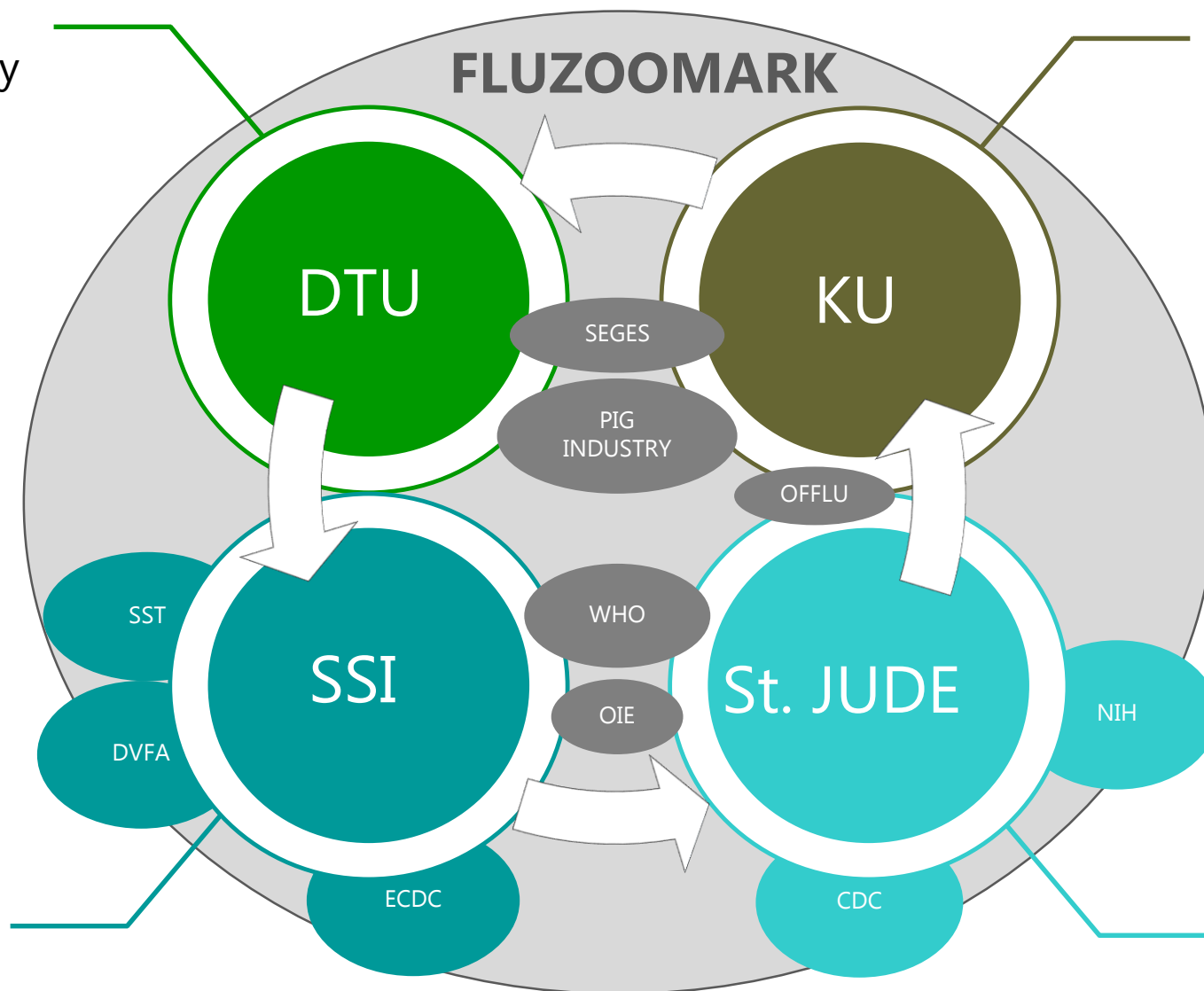
Experts human influenza and bioinformatics



Experts swine influenza and swine diseases



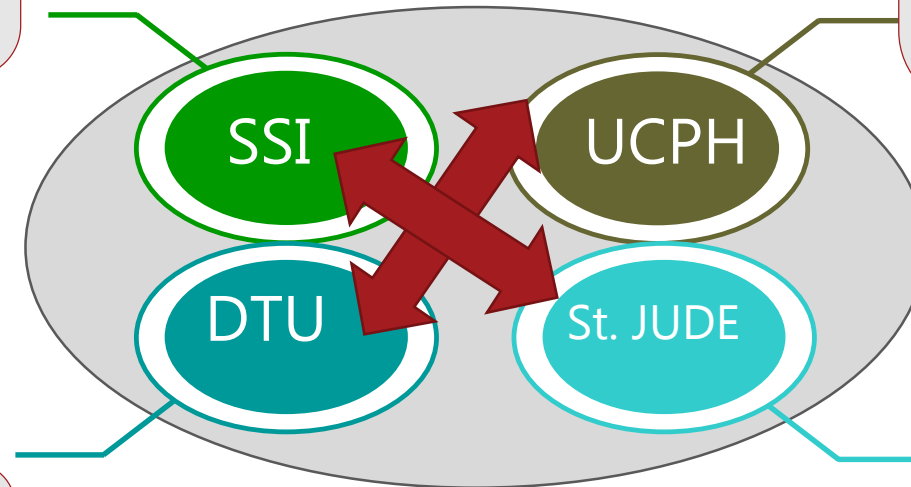
Experts animal models and human immunology



FLUZOOMARK Resources 60 million DKK 6 years (2020-25)

Co-applicant: Min 6 Mo per year
Post Doc: Bioinformatics
Post Doc: Vaccine development
PhD: Bioinformatics
PhD: Vaccine development

Project leader.: Min 6 Mo per year
Project coordinator: 12 Mo/year
Scientist: RG system 5 MO/year
Post Doc: Organoids etc
PhD: RG and Sequencing
PhD: In Vitro methods
PhD: In vivo and ex vivo methods



Min. 48 Mo
at St. Jude

Co-applicant: Min 6 Mo per year
Post Doc: Exp infections etc.
PhD: Innate immune responses
PhD: Proteases and other markers

Co-applicant: Min 3 Mo per year
Post Doc: Responses in humans

Min. 18 Mo
at St. Jude

Impact of the project

- **Direct outcomes**

- Identification and validation of markers for fast identification of zoonotic IAVs
- Vaccine stockpiles or seed viruses can be prepared – prevent/mitigate effect of pandemics
- Improved knowledge on the biology of IAV - high-impact scientific publications

- **Perspectives – spin offs**

- Establishment of a permanent One Health research centre at UCPH
- Increased research activities on IAV financed by other sources, including EU
- Form the scientific basis for the development of improved IAV vaccines and therapeutics
- Tools for research into the veterinary importance of influenza in animals (pigs, poultry, mink)

Thank you – questions, please

